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TESTS FOR THE ADULTERATION OF HUMAN MILK

BY

R. A. MILLER and R. W. B. ELLIS

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(RECEIVED FOR PUBLICATION JANUARY 26, 1953)

The necessity for testing human milk destined for milk banks in order to eliminate specimens which have been adulterated with water or cow's milk has been widely recognized since the introduction of such banks in 1910 (Mackintosh, 1947). In some centres, however, no tests for adulteration seem to be used, in spite of the fact that the mothers providing milk for these banks are not supervised between the time they express the milk and deliver it to the milk bank or milk bank official.

Various tests have been used to detect adulteration, and there is to this day no agreement on which are most reliable. The selection of tests in the past has depended partly on the efficiency of a test but also on other factors such as the speed and ease with which a test can be performed, the simplicity of the apparatus, the ease with which reagents and sera can be obtained, and financial considerations. It would appear therefore that the ideal test or combination of tests used in the detection of adulteration of human milk with water or cow's milk should be quick and easy to perform and preferably should not involve complicated or expensive apparatus. The test must be reliable and able to detect minor degrees of adulteration. With these criteria in mind the many tests recommended for the detection of adulteration have been reviewed and those which best fulfil the conditions selected for discussion. In addition an investigation has been made into the freezing point of women's milk; the value of assessing the freezing point or the electrical conductivity of women's milk for the detection of adulteration of the milk has been explored.

Review of the Literature

Since last century many methods of detecting the adulteration of women's milk have been devised. Usually one test appears no better than another and the tests are neither sufficiently sensitive nor reliable. This is probably because the physical and chemical properties of milk vary from case to case and even in a given individual.

At least six simple tests have been advocated for the detection of water added to women's milk. Two are based on the determination of a physical property of the milk, and three depend on its chemical composition. The sixth is a combination of the two tests, one involving a physical property and one a chemical property of milk. Of these tests based on physical properties, the first necessitates the estimation of the refractive index of the milk specimen in question. The interpretation of the results must be made cautiously because they vary for genuine milk, particularly if the sugar or solids-not-fat contained in the milk alter either under physiological conditions or on account of disease. Gnosspelius (1940) when criticizing the test says that it is necessary to obtain a control sample of milk reliably obtained from the woman under test. The refractive index of both the given milk sample and the control sample is made and the results compared. By this method 10% or more of added water can be detected (Kappeller and Gottfried, 1920; Zaribnicky, 1942). In the dairy world the refractive index is not a reliable test for detecting adulteration, and it therefore appears that the results of the refractometric test are unlikely to be reliable for the detection of adulterated human milk. The second test involves measurements of the specific gravity of the milk specimen. This is an unsatisfactory test because it is only suitable for detecting gross adulteration.

Of the three tests based on the chemical composition of milk, the first involves the estimation of its chloride content. From the results it is usually possible to detect large amounts of added water. The test, however, is not reliable or of practical value (Miller, 1949). In the second test both chloride and lactose content of the specimen are determined. From the results the chloride-lactose ratio is calculated. In the case of genuine human milk it is $0{\cdot}44 \pm 0{\cdot}015$. The ratio may be greater and approximate to that of cow's milk, $2{\cdot}23 \pm 0{\cdot}082$, if the milk is from women in the first month of lactation or from women with inadequate lactation. It is highly

unlikely, however, that such women would be donors to a milk bank (Keller and Mai, 1930). Milk adulterated with large amounts of water has a chloride-lactose ratio less than 0·425. The third test is dependent on the relatively high lactose and low albumin content of the milk to detect adulteration. From the tint which originates by a reduction of a copper salt solution by the lactose in the milk-serum and by the amount of oxide of iron necessary for a quantitative precipitation of albumin, Edelstein (1921) was able to ascertain whether or not the human milk had been mixed with 20 to 30% or more of water. This test, however, is not reliable.

The final test for the detection of added water involves the estimation of the specific gravity of the milk and its fat content. The data is then used to give a point on the chart devised by Ström (1939) or for a formula. From the position of the point on the chart or from the result obtained by a special formula it is possible to detect 30% or more of water added to the specimen.

It has been shown that it is difficult to detect milk samples to which water has been added. Probably the least unsatisfactory method is to measure the refractive index of the milk. Other methods which may be adopted involve the estimation of the specific gravity and the percentage of milk fat, or the chloride and lactose content of milk, or the lactose and albumin content of milk.

Many quick and easy tests for the detection of human milk adulterated with cow's milk are available. These tests have been placed in one of four groups for the purpose of description and discussion. Group 1 includes tests dependent on a physical property of the milk, Group 2 includes those tests which necessitate investigation of one or two constituents of the milk, tests in Group 3 require the estimation of the hydrogen ion concentration of the milk in question, while those in Group 4 entail a biological investigation. In Group 1 (physical properties) the ultra-violet light test has been widely used because it is possible to detect the addition of small amounts of cow's milk in this way. Human milk normally gives a blue and cow's milk a yellow luminescence. Unfortunately both false positive and false negative results are sometimes obtained by this method (Griebel, 1937; Kayser, 1938; Smith, 1942). Another test, involving the estimation of the refractive index of the suspected milk detects an adulteration with cow's milk of 20% or more provided a reliable sample of milk from the woman who is being investigated can be similarly tested and the two results compared (Kappeller and Gottfried, 1920; Zaribnicky, 1942).

The second group of tests necessitates either the qualitative or quantitative analysis of some constituent of the milk. In one test both the chloride and lactose are estimated (Keller and Mai, 1930; Moruzzi and Tanzi, 1931). From the results the chloride-lactose ratio is calculated; when the ratio exceeds 0·455 adulteration must be suspected. Twenty-five per cent. or more of cow's milk added to the sample is usually detected. Edelstein in 1921 introduced the lactose-albumin test which detects 20% or more of added cow's milk, but the author states that the results are unreliable. Umikoff in 1896 devised a method of detecting adulterated milk by adding ammonia to the sample and heating it to 60° C. The colour of the heated mixture depended on the amount of lactose and citric acid present in the milk. In this way the presence of 20% or more of cow's milk could be detected. The end-point of this test is sometimes indefinite and difficult to interpret. The xanthine-oxidase test (Rodkey and Ball, 1946) is a simple test and is based on the fact that cow's milk is rich in the enzyme, xanthine, while human milk has so little xanthine it is undetected by this test. Milk adulterated with 10% of cow's milk or more can be detected. Unfortunately the test is useless if the milk is boiled because the enzyme, xanthine oxidase, is destroyed.

In the third group of tests the hydrogen ion concentration of the milk under test is estimated by the addition of some indicator such as neutral red (Moro, 1912) nile-blue sulphate (Bauer, 1913; Solé, 1935) or haematoxylin (Smith, 1942). By these methods 20 to 30% or more of added cow's milk can be detected. On some occasions, however, the interpretation of the colour reaction can be extremely difficult, while in others fallacious results may be obtained because the milk has been kept too long before testing. Soxhlet-Henkel's test for titratable acidity results which are more reliable and informative (Eldson and Walker, 1942). By their method acidity over 2 degrees indicates adulteration with cow's milk provided the test is made on fresh milk (Kayser, 1935).

In the fourth group, tests involving the use of the anaphylactic response have proved impractical and the technical procedure of the complement fixation test far too complicated (Gnosspelius, 1940). The precipitation test, however, using specially prepared sera is very sensitive and reliable and can be quickly and easily performed. By means of this test 2% or more of added cow's milk can be detected. There is little doubt that this is the ideal test for the investigation of adulteration of human milk with animal's milk (Kayser, 1938; Urbach, 1938; Brakhage and Raettig, 1940; Gnosspelius, 1940). Unfortunately, at the present time the sera required for this test are

not available in Great Britain. Once they can be obtained it is unlikely that there will be any necessity to resort to any alternative procedure. Until then, however, it will be necessary to select at least one of the tests already mentioned for the detection of adulteration of human milk with cow's milk. It should be remembered, however, that no test except the precipitation test gives conclusive evidence of the type of animal milk which has been added to the human milk.

Investigation of Freezing Point of Women's Milk

Methods. A few comments about the apparatus and method for measuring the freezing point, electrical conductivity and chloride content of milk are necessary.

The cryoscope devised by Hortvet in 1921 is the generally accepted apparatus for determining the freezing point of cow's milk (Lyons and O'Shea, 1950). This apparatus was used for measuring the freezing point of women's milk. The method of standardization of the thermometers was that suggested by Aschaffenburg and King (1951) and the apparatus was operated as described by the Association of Official Agricultural Chemists (1930). A more rigid method of stirring the milk under test, tapping the thermometer and reading the depression of freezing point recommended by Aschaffenburg and King (1951) was adopted. Throughout the investigation, which lasted from April to August, 1952, the temperature of the room was noted to vary by 9° C. The freezing point of each specimen was recorded in degrees Centigrade. In no case was any allowance made for this variation or for the degree of acidity of the milk.

The electrical conductivity was measured with a commercial Wheatstone bridge; a U-shaped cell for holding the milk to be tested and two platinum electrodes were used in the circuit. The specific conductivity was calculated from the resistance for a given sample of milk and the cell constant for the apparatus. The results were all corrected to give the specific conductivity of the milk at 18° C. Full details of this type of investigation are given by Kermack and Miller (1951).

The chloride content of the milk was determined by the method described by Patterson (1928). Ten millilitres instead of 2 ml. milk were used for the titration because this gave more accurate results. The chloride content of the milk was calculated in terms of milligrams of sodium chloride per 100 ml. of milk.

Material. The investigation was made on milk samples obtained from 215 women who were apparently healthy, at some stage of lactation between the fourth day and twenty-fourth week. One hundred and seventy of these women provided one sample of milk each. Twenty-six women supplied one sample from each breast and each of these women gave her two samples on the same day. Nineteen women gave two samples each but these were taken at different stages of lactation. Thus a total of 260 samples of milk were obtained and examined. Almost invariably the milk was expressed into a specially prepared screw-capped jar after the baby had been fed. The size of each sample was approximately 30 ml. and it was stored in a refrigerator until tested. The test was performed within 24 hours of the time the milk was expressed. The freezing point was determined for each of the 260 samples and the electrical conductivity and chloride estimations were made on 245 samples.

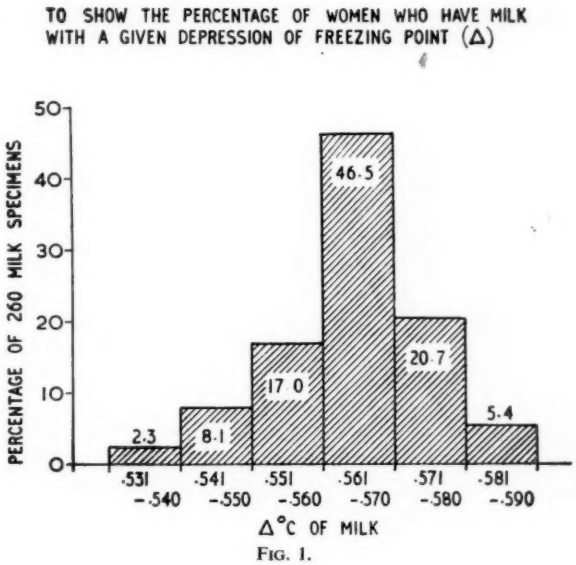

FIG. 1.

Results. The results of the investigation into the freezing point of human milk are given in Fig. 1. In this figure the percentage of the 260 samples of milk with a depression of freezing point between 0·531 and 0·540, 0·541 and 0·550, 0·551 and 0·560, 0·561 and 0·570, 0·571 and 0·580 and 0·581 and 0·590° C. has been adopted. The greatest number of results in any one group is 46·6% in the group ranging from 0·561 to 0·570, while the smallest number of results, 2·3% is in the group ranging from 0·531 to 0·540°C. The minimum and maximum depressions of freezing point obtained in this investigation are 0·531° C. and 0·586° C. respectively and the mean depression of the freezing point for the 260 observations is 0·564° C. These figures are of importance when using this test to detect the addition of water to milk.

TABLE 1

AVERAGE DEPRESSION OF FREEZING POINT OF MILK (△) TAKEN FROM WOMEN AT DIFFERENT STAGES OF LACTATION

	Week of Lactation								
	1	2	3	4	5–8	9–12	13–16	17–20	21–24
Average △° C.	0·563	0·566	0·570	0·563	0·563	0·563	0·569	0·567	0·566
No. of samples tested	90	85	12	4	36	16	6	6	5
No. of women tested	76	74	12	4	34	15	6	6	6

If the freezing point test is to be used to detect adulterated milk it is important to know whether the mean depression of the freezing point varies with the stage of lactation. Table 1 has been constructed to elucidate this point. In this table are the mean depressions of freezing point for milk samples taken from women in each of the following periods of lactation: the second, third, fourth, fifth to eighth, ninth to twelfth, thirteenth to sixteenth, seventeenth to twentieth and twenty-first to twenty-fourth weeks after childbirth. Set out with each mean are both the number of observations and the number of women tested. The means do not differ markedly from the mean of 0·564° C. for the entire investigation. In the two groups whose means differ most from the common mean the values have been based on relatively few observations and are, therefore, more liable to deviation. It appears, therefore, that there is no tendency for the depression of freezing point to alter significantly as lactation advances from the first to the twenty-fourth week after childbirth.

TABLE 2

COMPARISON OF DEPRESSION OF FREEZING POINTS (△) OBTAINED FOR SAMPLES OF MILK TAKEN FROM THE % TWO BREASTS

Case No.	△° C. Milk	
	Right Breast	Left Breast
1	0·550	0·560
2	0·540	0·540
3	0·541	0·549
4	0·550	0·551
5	0·543	0·543
6	0·549	0·544
7	0·550	0·550
8	0·560	0·560
9	0·555	0·551
10	0·553	0·550
11	0·550	0·560
12	0·555	0·558
13	0·568	0·560
14	0·552	0·560
15	0·549	0·543
16	0·550	0·551
17	0·540	0·548
18	0·530	0·539
19	0·562	0·552
20	0·542	0·550
21	0·554	0·550
22	0·560	0·560
23	0·549	0·551
24	0·561	0·555
25	0·549	0·545
26	0·530	0·530

In two further investigations the freezing point of milk samples taken first from the two breasts was compared, and second a comparison was made between two samples obtained from the same woman at different stages of lactation. Two series of women were investigated; the first comprised 26 women each of whom expressed milk from both breasts keeping each specimen separate. The freezing point of the milk from each breast was determined and the results recorded in Table 2. A difference between the two results for a given woman was generally noted. It was usually no greater than 0·004° C. which could be due to either a slight difference in the composition of the two samples or to experimental error. In 11 cases, however, the difference exceeded 0·004° C. an amount which could not entirely be accounted for by experimental error. Thus some variation in the composition of the two samples would seem to be the most likely explanation for the difference in the freezing points of milk from the same woman.

A series of 19 women were selected for the investigation into the effect of state of lactation upon the freezing point of their milk. These women provided two samples of milk each taken at a different period of lactation. The freezing points of the samples are recorded in Table 3 where it can be seen that the

TABLE 3

COMPARISON OF DEPRESSION OF FREEZING POINTS (△) FOR TWO SAMPLES OF MILK OBTAINED FROM THE SAME WOMAN AT DIFFERENT STAGES OF LACTATION

Case No.	Week of Lactation	△° C.	Week of Lactation	△° C.
1	1	0·565	2	0·582
2	1	0·554	2	0·565
3	1	0·565	2	0·575
4	1	0·561	2	0·565
5	1	0·549	2	0·576
6	1	0·543	2	0·555
7	1	0·563	2	0·562
8	1	0·565	2	0·567
9	1	0·561	6	0·564
10	1	0·566	6	0·555
11	2	0·564	2	0·565
12	2	0·585	3	0·570
13	2	0·565	3	0·554
14	2	0·575	7	0·565
15	3	0·563	6	0·565
16	3	0·555	7	0·550
17	3	0·565	13	0·574
18	6	0·563	10	0·556
19	10	0·575	17	0·572

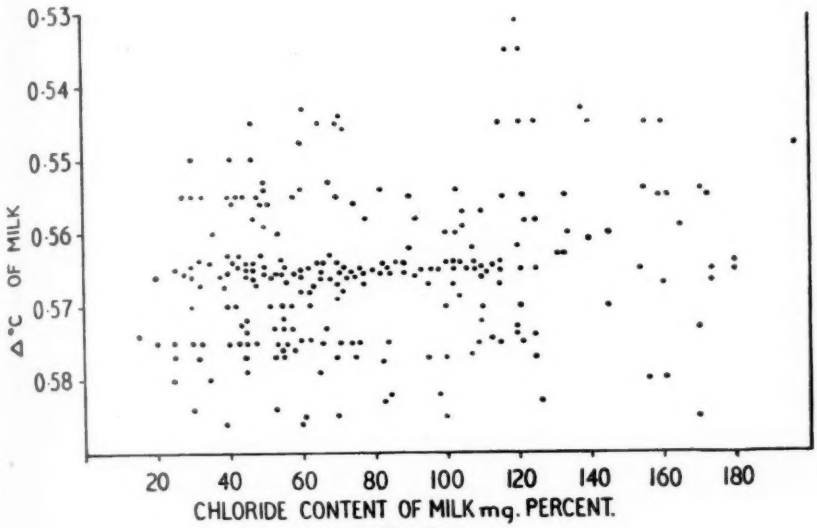

FIG. 2.

value obtained for the second sample may be either greater or smaller than that obtained for the first sample. The difference between the freezing points for the two samples from a given woman in some cases amounts to at least 0·005° C., an amount which can be explained by a change in the composition of the milk.

An investigation was made into the freezing point, chloride content and electrical conductivity of samples of human milk to determine whether any relationship existed between the freezing point and the other physico-chemical properties. Two hundred and forty-five milk samples were examined, on each of which the freezing point, chloride content and electrical conductivity were estimated. The results are summarized in Tables 4 and 5 where it is apparent that the average freezing point of milk samples with a low chloride content does not differ appreciably from that for milk samples with a high chloride content. The scatter graph (Fig. 2) shows that there is no relationship between individual values and depression of freezing point. From Table 5 it can also be seen that the average freezing point for milk of a low electrical conductivity does not differ appreciably from that for milk of a high electrical conductivity. The scatter graph (Fig. 3) shows that there is no relationship between individual electrical conductivity values and the depression of the freezing point. It is, therefore, apparent that there is no relationship between the depression of freezing point of milk and its chloride content or its electrical conductivity.

Freezing Point Test. The addition of water to cow's milk can be detected quickly and easily by determining the freezing point of the given sample. If water has been added the freezing point is higher than that of unadulterated milk. This result can be used to estimate the

TABLE 4

AVERAGE VALUE FOR THE DEPRESSION OF FREEZING POINT (△) FOR MILK OF DIFFERENT CHLORIDE CONTENT

Chloride Content (mg.%)	No. of Specimens	Average △° C.
1–50	64	0·563
51–100	105	0·567
101–150	58	0·564
151–200	18	0·562

TABLE 5

AVERAGE VALUE FOR THE DEPRESSION OF FREEZING POINT (△) FOR MILK OF DIFFERENT ELECTRICAL CONDUCTIVITY

Electrical Conductivity (10^{-5}ohm^{-1}cm.$^{-1}$)	No. of Specimens	Average △° C.
151–200	85	0·566
201–250	94	0·566
251–300	53	0·562
301–350	13	0·563

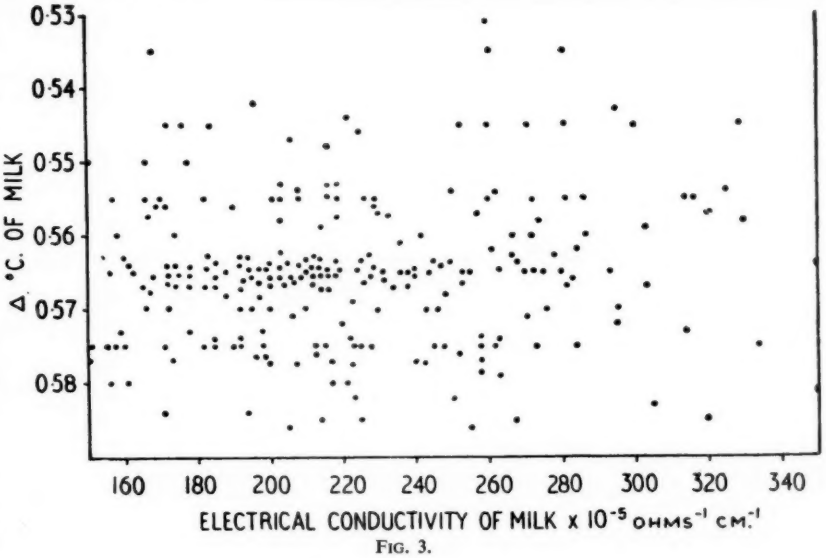

FIG. 3.

approximate amount of water added to the specimen by means of the formula

$$W = \frac{100\ (T—T')\ \%}{T}$$

recommended by the American Association of Official Agricultural Chemists where W is the amount of water added, T′ is the freezing point depression of the sample, and T is the freezing point depression of genuine milk (or an average for genuine milk), and though the results obtained by the formula are a slight over-estimation of the percentage of added water, they are sufficiently accurate for practical purposes (Elsdon and Walker, 1942).

A series of observations were made on human milk, to which had been added varying amounts of water, to determine whether the above formula was of value in the estimation of adulteration of women's milk with water. A quantity of women's milk was divided into four parts, and each part was adulterated with 3·3, 16·6, 33·3 and 66·6% of water respectively. The freezing point of each specimen (x) was estimated by the method already described and recorded in Fig. 4. The theoretical freezing point (·) of each specimen was calculated from the formula and lay on a straight line connecting the depression of freezing point of unadulterated milk with the freezing point of water (see Fig. 4). The comparison of the experimental-theoretical values for a given dilution of milk showed that they were either the same or the experimental value was slightly higher than the theoretical value. It was also apparent from Fig. 4 that if the amount of added water were calculated from the theoretical value it might be as much as 2% in excess of the correct amount. This difference is not of practical importance. Therefore, the suggested formula, based on the principle that the raising of the freezing point of milk by the addition of water is proportional to the amount of added water, is of practical value in calculating the degree of adulteration of women's milk. Similar results have been obtained for dilution of cow's milk and have been explained by Elsdon and Walker (1942).

The sensitivity of the freezing point test is partly dependent upon the range of freezing point depression for genuine human milk; this range is 0·531 to 0·586° C. Since the addition of water to milk raises the freezing point, the percentage of water which must be added to milk with the lowest freezing point, 0·586° C., to raise it above the highest freezing point, obtained for normal unadulterated milk is a measure of the test's sensitivity. This value is 9·75%. Therefore, the freezing point test will detect 10% or more of water added to women's milk. If the test is used for milk which has a higher freezing point than 0·586°C. less than 10% adulteration can be detected.

The Electrical Conductivity Test

The electrical conductivity test for detecting adulteration of women's milk has not hitherto been described. The measurement of electrical conductivity is simple (Kermack and Miller, 1951) but the interpretation of the results, together with the

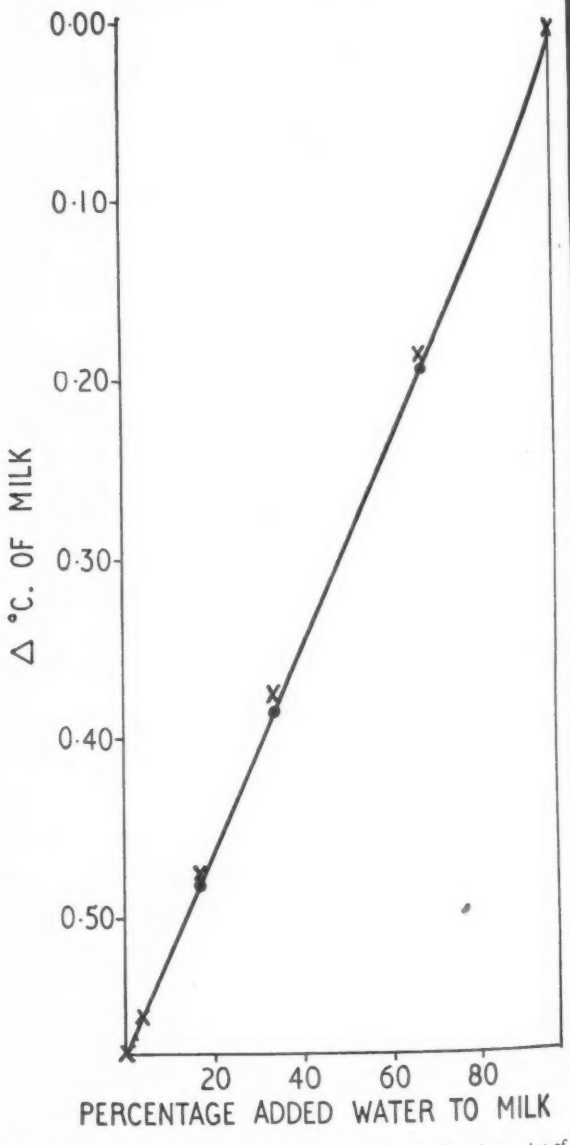

FIG. 4.—To show the changes in the depression of freezing point of milk △ which occurs when it was watered.
(X) represents the depression of freezing point of mixtures based on practical observations while (·) represents the depression of freezing point based on theoretical calculations.

sensitivity of the test and its fallacies require careful consideration. It is, therefore, necessary to consider the test as a method for the detection of both added water and added cow's milk. The addition of water to human milk reduces its electrical conductivity. The reduction is almost proportional to the amount of added water. Usually the experimental value for a given dilution of milk is 1-9% less than the theoretical electrical conductivity value (Fig. 5). The difference between the measured and the theoretical values

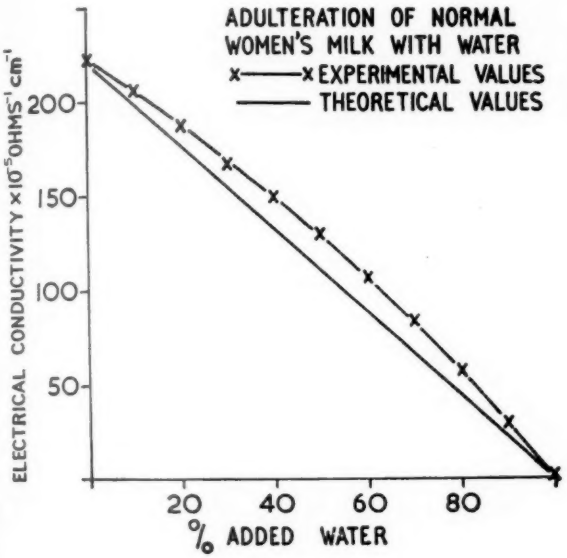

FIG. 5.

is partly due to the change in the viscosity of the milk and to the increased dissociation of certain electrolytes in the diluted milk.

The amount of added water which can be detected by the electrical conductivity test depends on the initial electrical conductivity value of the milk. This ranges from 210 to 150×10^{-5}ohm^{-1}cm.$^{-1}$ for women lactating adequately in the second to fifth month of lactation (Miller, 1951). Since the values fall when water is added, milk with the highest electrical conductivity value, 210×10^{-5}ohm^{-1}cm.$^{-1}$, will require the maximum amount of water (33%) to lower its conductivity below the minimum value of 150×10^{-5} ohm^{-1}cm.$^{-1}$. Therefore it follows that by means of the test at least 33% added water can be detected in milk from mothers with adequate lactation in the second to fifth month of lactation. Occasionally the electrical conductivity test fails to detect 33% of added water because the genuine milk has a conductivity value greater than 210×10^{-5}ohm^{-1}cm.$^{-1}$. This, however, is a relatively rare occurrence because such milk is usually obtained from women with inadequate lactation and they would therefore not be donors to a milk bank.

By using the electrical conductivity test it is possible to detect human milk which has been adulterated with cow's milk. It has been shown that the addition of cow's milk raises the conductivity of human milk, and that it is most unusual for the electrical conductivity of milk obtained from women lactating adequately in the second to fifth month of lactation to exceed 210×10^{-5}ohm^{-1}cm.$^{-1}$. If, therefore, a value greater than this is obtained, the possibility of inadequate lactation and of adulteration of the milk must be considered. To obtain a conductivity value greater than 210×10^{-5}ohm^{-1}cm.$^{-1}$ as much as 23% of cow's milk may require to be added to human milk (Miller, 1949). To prove, however, that the increased conductivity value was due to adulteration of the human milk with cow's milk rather than to inadequate lactation would entail further investigation and probably involve test-weighing the mother's infant over a period of 24 hours.

Comments

The practical value of the depression of the freezing point as a test for the adulteration of women's milk with water depends not only on the ease with which it is estimated, but also on the accuracy of the result and to possible variations arising from mother to mother and the stage of lactation. Unfortunately previous research on this subject (Winter, 1896; Winter and Parmentier, 1904; Wardlaw and Dart, 1926) has been made with different types of apparatus (e.g. Beckman's thermometer) and technical procedures which influence the freezing point of a given milk sample. These results are not strictly comparable with those obtained in the present investigation and no conclusions can be drawn as to the accuracy of the results. It has been stated, however, by Wardlaw and Dart (1926) that the individual values in their series varied from −0·545 to −0·622° C. This is a greater variation than that of −0·531 to 0·586° C. obtained in the present series of observations. This smaller variation increases the value of the freezing point test as a means of detecting adulteration since the amount of water which must be added to alter normal women's milk of the lowest freezing point above that of the highest normal value is less if the variation is small. Wardlaw and Dart (1926) noted a tendency for the freezing point to rise as lactation advanced, but the mean values for various stages of lactation differed very little from the mean value for all the observations. The depression of freezing point in the present series of observations was not significantly affected

by the stage of lactation. The test, therefore, should prove equally satisfactory at whatever stage of lactation it is used. The same authors stated that milk from women aged 23 to 26 had values which on the average were slightly higher than that for younger or older women. It is unlikely that the difference between the two groups of women is significant.

Before any definite statement as to the value of the test as a means of detecting adulteration of human milk with water is made a further series of observations made by the same method is desirable. It appears, however, that the test is sensitive and the technique easy and not too time consuming. It would appear equally sensitive at whatever stage of lactation it is performed and not markedly affected by the variations normally found in milk of apparently healthy mothers. The only other test used for the detection of water added to human milk which has comparable sensitivity is the refractometric test. This test, however, requires two specimens from the woman under investigation, one of which must be known to be unadulterated. This latter sample may not be easily obtained. The fact that the freezing point test is a quantitative one and can be done with one sample of milk means that it is preferable to the refractometric test.

The electrical conductivity test as a detector of added water to human milk is probably as efficient as most tests used for this purpose, but it is only suitable for detecting 33% or more of added water to milk obtained from a woman who has passed her puerperium and is lactating adequately. The test is, however, more rapidly and easily performed than either the specific gravity test or the chloride-lactose test, both of which detect similar degrees of adulteration. The refractometric test is possibly more efficient but more time consuming.

The electrical conductivity test is of little practical value for the detection of human milk to which cow's milk has been added. This is because it may give false positive results and to eliminate the possible error would involve much work. Many other tests for adulteration with cow's milk also give unreliable results. The precipitation test, however, is reliable and most satisfactory. It is capable of detecting 2% of adulteration. The refractometric test is another reliable test but only for the detection of 20% or more of added cow's milk.

The most accurate method of investigating the possible adulteration of women's milk would appear to be the testing of the milk for acidity along the lines advocated by Soxhlet-Henkel (SH). Samples with an acidity not greater than 2 degrees (SH) are regarded as fresh. The freezing point of these samples should be estimated to detect adulteration with water. Samples with an acidity exceeding 2 degrees (SH) are either sour or contain cow's milk. These should be subjected to the precipitation test. Application of the freezing point test to samples of milk with an acidity greater than 2 degrees (SH) requires further investigation.

Summary

The depression of freezing point of human milk has been investigated. Estimations have been made on 260 samples of milk taken from 215 apparently healthy women between the fourth day to the sixth month of lactation. The results showed that the depression of freezing point ranged from 0·531 to 0·586° C. The mean value for all the observations was 0·564° C. The freezing point for samples taken from the two breasts frequently differed, as did the freezing point for samples taken at different times from the same woman. The mean values for samples taken from women at various stages of lactation did not differ appreciably and certainly did not suggest that the freezing point of milk tended either to rise or fall as lactation progressed.

There was no relationship between the depression of freezing point of women's milk and the chloride content or the electrical conductivity of the milk.

It has been shown that it is possible to detect the addition of 10% or more of water to human milk by using the freezing point test. From the result it is also possible to state the approximate degree of adulteration. The reliability of these conclusions depends upon the milk being fresh.

The use of the electrical conductivity test to detect adulteration of human milk with either water or cow's milk has been described. The test is recommended for the investigation of possible adulteration with water should both the freezing point and the refractometric tests be impracticable. The electrical conductivity test does not appear to be of practical value for the detection of adulteration of human milk with cow's milk, there being at least three more suitable tests for this purpose.

A scheme for testing human milk involving the freezing test and precipitation test along with a quantitative estimation of acidity has been suggested.

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PULMONARY ATELECTASIS IN YOUNG CHILDREN

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The importance of atelectasis in the production of bronchiectasis has been frequently discussed during the past 15 years.

Theoretical considerations suggest that an obstruction preventing aeration of a lobe or segment of affected lung may be due to plugging of the bronchial lumen, alterations in the bronchial wall, or extrabronchial compression (Anspach, 1939). Moreover it would appear probable that the very narrow lumen of the bronchi and the relative weakness of their walls in infancy are factors which make absorption collapse more probable in respiratory lesions at this age.

Chevalier Jackson (1950) has produced a comprehensive list of almost every possible cause of absorption collapse. Brock, Cann and Dickinson (1937) have demonstrated the importance of extrabronchial compression by enlarged lymphatic nodes and Lander and Davidson (1938) by both experimental and clinical methods showed how secretions or solid matter within a bronchus might cause obstruction and lead to atelectasis and bronchiectasis.

Several clinical conditions have been widely recognized as precursors of absorption collapse. Particularly careful investigation has been made in the case of primary tuberculosis (Brock *et al.*, 1937; Graham and Hutchison, 1947; Hutchison, 1949; Macpherson and Lutwyche, 1950; Jones, Peck and Willis, 1946) and pertussis (Nicholson, 1949; Lees, 1950). Pneumonia and upper respiratory infections find a place in all lists of general causes of collapse (Field, 1949; Anspach, 1939; Paulson and Shaw, 1949; Oswald, 1947), and pneumonia has received special attention (Wyatt, 1942).

In the present series, 77 children aged 5 years or under, suffering from lobar or segmental atelectasis, were studied at the Duchess of York Hospital for Babies during the period February, 1950, to December, 1952. The children were seen both as in-patients and out-patients, and all were followed in the out-patient department until re-aeration had taken place and for at least six months thereafter, or until the establishment of bronchiectasis had been confirmed.

Investigations

Clinical Examination. Large areas of collapse producing typical physical signs could be detected clinically but small areas of segmental collapse were usually only discovered radiologically. Clinical assessment was the most important means of deciding the underlying cause of the collapse.

Radiology. In all cases serial antero-posterior and lateral films were taken and confirmed, where necessary by screening. The radiological appearance of lobar and segmental collapse has been described in detail by Foster-Carter and Hoyle (1946) and Robbins and Hale (1945) and in most cases the x-ray shadow could be fitted into one or other category which they describe. The value of screening in the demonstration of a collapse of the right middle lobe and occasionally of the left lower lobe was manifested frequently. Positive x-ray findings were considered essential for the diagnosis of collapse.

When the collapse persisted for a year or longer bronchography was performed and repeated if necessary at yearly intervals. Lipiodol was always used as the contrast medium; a general anaesthetic was given after preliminary drainage.

Laboratory Investigation. Examination of the blood has not proved of any value in the diagnosis or prognosis of the collapsed lobe itself but white cell counts and estimations of the erythrocyte sedimentation rate have in many cases helped to throw light on the lesion causing the collapse and its state of activity. Bacteriology has in some cases shown the presence of a similar organism in nasal swabs, antral washings and pus from bronchial aspiration, but these results are not sufficiently extensive to warrant any definite conclusions.

Tuberculin Tests. These were performed in every case to a dilution of 1 in 100 O.T. and repeated if necessary.

Otorhinological Investigations. Radiography of the

sinuses was frequently undertaken but proved of little diagnostic help; a continuous purulent nasal discharge seems to be a much more important positive finding. Antral lavage was performed, if necessary more than once, and bacteriological examination of the results in these cases has been useful. Tonsils and adenoids were removed when necessary. Bronchoscopy was performed in 13 cases, and was found of great value in diagnosis but not in treatment.

Treatment. This must be directed towards two ends, treatment of the underlying cause and re-expansion of the collapse.

It is not within the scope of this paper to discuss how the factors causing the collapse should be dealt with, but it must be emphasized that this line of attack is probably the most important way of ensuring eventual re-expansion. Postural drainage, tapping and adequate physiotherapy, where there is no extramural compression, are the main weapons in dealing with the atelectasis. Bronchoscopy is useful from the diagnostic point of view, but except in cases of infective atelectasis or post-anaesthetic inhalation, when the child is usually too ill for it to be attempted, does not seem to be of much advantage. Gans (1952) has undertaken routine bronchoscopy in 50 cases with immediate results slightly better than in this series, but final figures for eventual re-expansion or bronchiectasis may prove to be similar.

Results

It was found that the diseases predisposing to atelectasis fell into six main groups; acute infective atelectasis, primary tuberculosis, pneumonia, asthma, pertussis and upper respiratory infection.

Tables 1, 2 and 3 show the various groups of diseases in relation to age at onset, lobes affected, and duration and outcome of the collapse. For purposes of clarification it has been found expedient to deal with 100 'incidents' rather than the 77 cases, as in many of these children more than one factor might be at work, either simultaneously or consecutively: for the purpose of tabulation, when two or more lobes or segments were collapsed at the same time both have been noted, and recurrent collapses have been counted each time they occurred; thus there is a total number of 129 lobes involved.

Acute Infective Atelectasis. This condition has been described by Scadding (1948) and by Jersild and Riskaer (1951), and it is probable that as more recognition is paid to it as an entity more cases will be so described.

There were nine incidents in this group; all the children were under 1 year at the onset, and six were under 3 months. The right upper lobe was affected in eight cases and in the ninth, segments of the left upper and middle lobes were affected simultaneously. In all cases re-aeration occurred in a year or less.

The typical history is that of an acute upper respiratory infection for a few days, followed by a sudden onset of respiratory distress: a diagnosis of bronchopneumonia is frequently made as the physical signs of a segmental collapse may be difficult to elicit in a small baby. It is suggested that the frequent involvement of the right upper lobe in these cases is due to the supine position of the infant, and the actual cause of the collapse is plugging of the bronchial lumen by viscid mucus or mucopus.

Four of the patients in whom there was right upper lobe collapse suffered from dorsal scoliosis, and the point has been raised as to which was the original lesion. It is quite possible that an idiopathic scoliosis might lead to twisting of the trachea and main bronchi and facilitate blocking of a bronchus by plugs of secretion; on the other hand the scoliosis might be of thoracogenic origin. All these spines were straight by the time the patients were 1 year old, re-aeration taking place first.

One other case was of particular interest. She was a twin and was admitted at the age of 4 months, having had a 'cold' for a week. The other twin had died suddenly five days previously and necropsy revealed plugs of mucopus blocking the trachea and right main bronchus. The surviving twin had a segmental collapse of the left upper and lower lobes, which became re-aerated within four weeks under treatment with penicillin and oxygen.

Primary Tuberculosis. This has long been recognized as a cause of absorption collapse in childhood. Grounds for diagnosis in this group were a positive Mantoux reaction associated with one or more confirmatory features including other manifestations of active tuberculosis, the presence of tubercle bacilli in gastric washings, recent Mantoux conversion, symptoms of illness in a child under 2 in whom the previous state of the tuberculin test was not known, or recent contact with active tuberculosis.

There were 15 incidents in this group. It is recognized that an incidence of 15% is probably not a truly representative proportion due to primary tuberculosis and that a large number of children with this condition may not be seen at a children's hospital but may attend the local chest clinic.

Only two children in this group were under 1 year of age at the onset. Twenty-three lobes were involved in the 15 incidents, and the high ratio of lobes per patient is largely due to the fact that in two cases the whole left lung was originally involved, and in two other cases different segments on the right side were recurrently affected. All lobes were involved but the

TABLE 1
AGE AT ONSET

Disease	Number of Incidents at Age of Onset										Total
	Under 1 Year					Over 1 Year					
	Age in Months				Total						
	0–2	3–5	6–8	9–11		1	2	3	4	5	
Acute infective atelectasis ..	6	2		1	9						9
Primary tuberculosis	1	1			2	3	3	3	4		15
Pneumonia	2	1		5	8	2	1	2	1		14
Asthma		1	2	1	4	1	3	4	1		13
Pertussis		2		2	4	2	4	1	1	1	13
Upper respiratory infections ..	2		2	6	10	5	8	4	5	4	36
	11	7	4	15	37	13	19	14	12	5	100

TABLE 2
LOBES AFFECTED

Disease	No. of Incidents	Lobes Affected								Total Lobes	Ratio R : L
		Right Side				Left Side					
		U.	M.	L.	Total	U.	Ling.	L.	Total		
Acute infective atelectasis ..	9	8			8	1		1	2	10	4·0 : 1
Primary tuberculosis.. ..	15	5	6	3	14	3	2	4	9	23	1·6 : 1
Pneumonia	14	3	4	2	9			7	7	16	1·3 : 1
Asthma	13	4	7	4	15	2		4	6	21	2·5 : 1
Pertussis	13	1	7	4	12	1		5	6	18	2·0 : 1
Upper respiratory infection..	36	5	17	6	28	1		12	13	41	2·2 : 1
	100	26	41	19	86	8	2	33	43	129	2·0 : 1

U = upper. M = middle. L = lower. Ling. = lingula.

TABLE 3
DURATION AND OUTCOME

Disease	Re-aeration								Pending			Bronchiectasis Confirmed					No. of Incidents
	Under 1 year					1-3 years						Under 2 years		2-4 years			
	Under 6 months			6-11 months													
	Under 1/12	1-2/12	3-5/12	6-8/12	9-11/12	1	2	3	Under 6/12	6-11/12	1 yr.	1-1½	1½-2	2	3	4	
Acute infective atelectasis	2	2	2	2		1											9
Primary tuberculosis	1	2	4	1	1	2				2	1				1		15
Pneumonia	1	3	2	1	1					1		1	1	2	1		14
Asthma	2	4	4							1	1		1				13
Pertussis		4	1	1			1			1	1		1	2		1	13
Upper respiratory infection	2	9	8	4		2	1	1		2	1		2	2		2	36
	8	24	21	9	2	5	2	1		7	4	1	5	6	2	3	100
	72% re-aerated. 53% re-aerated in less than 6 months.											17% developed bronchiectasis.					

right middle lobe was the most frequently affected and the ratio right to left was 1·6 : 1.

Re-aeration has taken place in 11 of these children, in seven cases in under six months. One case has developed bronchiectasis in the left lower lobe and lingula and three others are still under observation.

Brock *et al.* (1937) and Hutchison (1949) have shown the importance of glandular enlargement in causing compression of bronchi and obstructive atelectasis in these cases, although it has also been shown by Daly, Brown, Lincoln and Wilking (1952) that oedema of the bronchial walls, plugging with debris, or stenosis may also play a part. The fact that re-aeration took place in a comparatively short time in almost half of the cases in this series suggests that the precipitating factor was one of short duration acting where the bronchial lumen was already narrowed. 'Wheezing' has long been recognized as one of the symptoms of primary tuberculosis when atelectasis is present, but by analogy with other conditions in which this symptom is observed it is probably due to oedema or spasm of the whole bronchial tree, rather than a manifestation of local collapse. When present it has been treated effectively with anti-histaminics: in several cases these asthma-like symptoms persisted after the collapse had disappeared and all signs of tuberculous activity had cleared.

Pneumonia. There were 14 incidents in which pneumonia rather than acute infective atelectasis appeared to be the main cause of collapse. Eight of the patients were under 1 year of age at the onset, a proportion higher than that of the overall figures. Sixteen lobes were affected by atelectasis and the left lower lobe was the most frequently involved. The ratio of right to left collapse was 1·3 : 1. Eight patients have shown re-aeration (six in less than six months) and in five cases bronchiectasis has developed. Two are still under observation.

Asthma. There were 13 incidents in this group. Four of these cases were purely allergic in origin, being associated with other manifestations of allergy, and showing at one time or another eosinophil counts greater than 1,000 per c.mm. Eight were infective in origin, being associated with bouts of upper respiratory infection and pyrexia, and the allergic symptoms responded dramatically to anti-histaminics; in two cases the upper respiratory infection was sufficient to cause chronic enlargement of the hilar glands. In only one of these cases was the eosinophil count greater than 1,000 per c.mm. In the thirteenth case the sensitizing agent may have been tuberculin. Of asthma leading to collapse, bouts occurred several times in the presence of enlarged tuberculous hilar glands, and the eosinophil count was over 1,500 per c.mm. The age distribution appeared to follow the general pattern.

Twenty-one lobes were involved, illustrating the ubiquitous nature of the underlying cause. In four cases one particular segment showed transient recurrent collapses, while in four other cases different lobes were involved in different episodes. The ratio of right to left collapses was 2·5 : 1.

Re-aeration of the collapse within six months has taken place in all cases except one: in this child, who developed bronchiectasis of the right middle lobe, the asthma was associated with chronic upper respiratory infection and persistent hilar adenitis, and was probably a secondary manifestation.

Pertussis. Thirteen incidents are reported but it is realized that the distribution is not truly representative, as in all but one case the children attended on account of a cough persisting for some weeks after the onset of pertussis, and thus a number of transient collapses sustained during the acute phase of the disease must have been missed.

The incidence of pertussis in all the children under observation was as follows:

Not had pertussis	35 cases
No record	17 cases
Known to have had pertussis, but not considered significant	5 cases
Developed pertussis during period of observation, but did not develop atelectasis	7 cases
Pertussis thought to be cause of collapse	13 cases
	77 cases

The age at onset in this group tended to follow the general pattern.

Nineteen lobes were involved, the right middle being the most frequent, and the right to left ratio was 2·0 : 1. Re-aeration has taken place in seven cases, in five within six months. Four children have developed bronchiectasis. Two cases are still under observation.

Upper Respiratory Infection. By far the largest number of incidents, 36, fell into this category.

In six of the cases acute upper respiratory infection was present. In the remaining 30 cases the infection was chronic; 17 had chronic enlargement of the hilar glands, demonstrated radiologically, and persisting over long periods; 13 had chronic sinusitis or infected tonsils and adenoids without obvious glandular enlargement. All these patients had negative tuberculin reactions.

The distribution of age-groups at the onset of the collapse followed the general trend.

Forty-three lobes were involved, the right middle being the most commonly affected and the left lower being next in incidence. The right to left ratio was 2·2 : 1.

Re-aeration has taken place in 27 cases, in 19 in

less than six months. Six have developed bronchiectasis. Three are still under observation.

Discussion

The value of this series of cases lies in the fact that it is a study of a particularly young age-group and that most patients (although not all) have been followed from the onset of the collapse and the diagnosis is not retrospective.

Table 4 illustrates and compares the findings of previous workers in dealing with atelectasis and bronchiectasis.

Oswald (1947) described 50 cases of collapse involving the lower lobes in a group of very young children. He found pneumonia to be the commonest cause, and cited one case of infected antra, three of primary tuberculosis and seven of pertussis. He was dealing only with lower lobes and thus the series is not truly representative; it is one of the few in which a left to right preponderance was observed.

Field (1949) described 272 cases of atelectasis in which 157 did not show bronchiectasis. Of these she ascribed the cause as pneumonia in 9·6%, pneumonia with pertussis or rubeola 10·8%, pertussis alone 14·7%, asthma and bronchitis 7·8%, upper respiratory infection, insidious or not specified, 43·7%. The right to left ratio was 1·56 : 1.

Paulson (1949) described 32 cases of lobectomy for atelectasis of the right middle lobe in an older age-group; 15 of these patients had simple glandular enlargement and in eight others the nodes were calcified and probably tuberculous.

In the urban conditions under which most of the patients described in this paper live a high incidence of upper respiratory infection is to be expected, and it would appear to be a precipitating and perpetuating factor in a large proportion of cases of atelectasis.

McLaurin (1935) has shown that iodized oil introduced into the nasal sinuses can be seen radiologically to find its way into the lungs within 24 hours, and he also demonstrated in animals a lymphatic spread to the hilar glands of a mixture of indian ink and tubercle bacilli injected into the upper respiratory tract. It thus seems quite feasible that chronic upper respiratory infection of whatever nature may lead to gross hilar lymphadenopathy often associated with constant dripping of infected material into the trachea. Indeed in many cases this has appeared to be the only explanation of the presence of a collapsed lobe, and in some cases has been the only factor in the production of bronchiectasis. In this series the fact that the right middle lobe (41 times) and the left lower lobe (33 times)

TABLE 4
COMPARISON WITH PREVIOUS SERIES

Author	Date	Atelectasis or Bronchiectasis	Subjective Underlying Pathology	No. of Cases	Ratio R : L
Graham and Hutchison ..	1947	Atelectasis	Primary tuberculosis	45	2·00 : 1
Hutchison	1949	Atelectasis	Primary tuberculosis	30	1·73 : 1
Macpherson and Lutwyche ..	1950	Atelectasis	Primary tuberculosis	39	3·30 : 1
Daly *et al.*	1952	Atelectasis	Primary tuberculosis	43	3·30 : 1
Nicholson	1949	Atelectasis	Pertussis		1·89 : 1
Lees	1950	Atelectasis	Pertussis	65	0·93 : 1
Oswald	1947	Atelectasis	All causes lower lobes only	50	0·69 : 1
Field	1949	Atelectasis	All causes	272	1·56 : 1
Raia	1938	Bronchiectasis	All causes	33	0·89 : 1
Perry and King	1940	Bronchiectasis	All causes except tuberculosis	400	0·78 : 1
Diamond and Van Loon ..	1942	Bronchiectasis	All causes	75	1·08 : 1
Jones, Peck and Willis ..	1946	Bronchiectasis	Primary tuberculosis	24	1·00 : 1
Schmidt	1947	Bronchiectasis	All causes except tuberculosis	158	0·82 : 1
Field	1949	Bronchiectasis	All causes	160	0·85 : 1
Whitwell	1952	Bronchiectasis (*a*) follicular (*b*) atelectatic	All causes	(*a*) 160 (*b*) 21	(*a*) 0·35 : 1 (*b*) 2·00 : 1
Griffiths	Present series	Atelectasis	All causes	77	2·00 : 1

were the most frequently affected by atelectasis suggests the importance of glandular enlargement associated with several of the precipitating diseases.

Except for Oswald's (1947) series of collapsed lower lobes and Lees' (1950) series of collapse in pertussis, all reported series of cases of atelectasis have shown a preponderance of right to left in ratios varying from 1·56 : 1 to 3·30 : 1. The reverse condition would appear to hold for cases of bronchiectasis. Right to left ratios varying from 0·35 : 1 to 0·89 : 1 have been reported by all workers except in a series due to tuberculosis reported by Jones *et al.* (1946) where the ratio was 1 : 1, and Diamond and Van Loon's (1942) series in which the ratio was 1·08 : 1.

Whitwell (1952) divided bronchiectasis into three types: follicular, atelectatic and saccular. Atelectatic bronchiectasis shows a similar distribution to that of atelectasis and follicular bronchiectasis a very marked left-sided preponderance.

In this series 11 children developed bronchiectasis in 15 lobes. The right middle was affected four times, the lingula twice and the left lower lobe nine times. Thus approximately one-tenth of right middle lobes affected became bronchiectatic, and a quarter of left lower lobes. In the majority of cases reaeration took place within six months, and this was particularly true when the cause of the collapse was of a transient character such as a plug of mucopus in infective atelectasis or oedema of the bronchial wall in asthma.

The longer the collapse persists the more probable becomes the onset of bronchiectasis, partly because of the duration of dilatation and partly because of the increased risk of infection. Most workers emphasize the importance of infection in causing irreversible bronchiectasis. It would appear that the process of dilatation is reversible (Lander and Davidson, 1938; Field, 1949) and that it is only when destruction of muscle and elastic elements in the bronchial wall takes place that the bronchiectasis becomes irreversible (Engel, 1947). Of these 77 cases, 11 children, i.e., 1 in 7, developed bronchiectasis and the highest incidence was in those conditions, pneumonia (1 in 2·8), pertussis (1 in 3·75), and upper respiratory infection (1 in 6), where infective elements were the greatest.

Summary

Atelectasis in 77 children aged 5 years and under has been described.

The age of onset, cause and duration of the collapse have been discussed in detail, with special reference to the importance of upper respiratory infection.

The place of atelectasis in the aetiology of bronchiectasis has been considered in relation to the figures produced by other workers.

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ATYPICAL PNEUMONIAS IN CEYLONESE CHILDREN

BY

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Although cases of primary non-bacterial pneumonia of unknown but probable viral origin have been reported from Europe and America only meagre references to this condition have been made in Indian medical literature. Shone and Passmore (1943) have referred to an outbreak of pneumonitis associated with autohaemagglutination in Indian army personnel. No such cases have yet been reported from the island of Ceylon. The purpose of this paper is to record nine cases which conform to the description of 'atypical' pneumonias reported by workers in other countries (Golden, 1944; Dingle, 1947; Parker, Jolliffe and Finland, 1947; Scadding, 1951).

The diagnosis of the first two cases was made at necropsy, and, as a result of these findings, subsequent cases, where the clinical picture differed from that of bacterial pneumonias, were carefully investigated, particular attention being paid to the estimation of cold agglutinins in the serum and to radiological changes in the lungs.

Clinical Features

The main clinical features were not specific, and in the absence of other investigations the diagnosis might have been influenza, bronchitis or acute respiratory infections. The onset was insidious, usually with a cough, and the temperature ranged from 98·4° F. to 105° F. The cough was not troublesome in most of the cases.

Physical signs consisted of râles and rhonchi of various tones, intensities and pitches, heard all over the lungs. The duration of the illness ranged from four to 144 days with an average of 28·3 days. If three very prolonged cases, lasting 39, 150 and 23 days respectively (the last complicated by meningitis) are excluded, the average period of illness is reduced to 7·8 days.

Laboratory Investigations

Leucocyte Count. Absence of a leucocytosis was a feature in all except two cases, but in all except one, sulphonamide drugs had been given before the count was done. In the one exception, a baby 3 months old, the total leucocytes were 17,600 per c.mm. in the first week of the illness, though the polymorphonuclears were only 31% and the lymphocytes 69%.

Cold Agglutinins. In five out of six cases the titre ranged from 1 in 64 to 1 in 256; the sixth read 1 in 32. Although this child was resistant to all antibiotics, including aureomycin, the x-ray appearances were suggestive of atypical pneumonia.

Radiological Appearances

Opacities were seen in all zones. In some cases, the shadows were limited to the upper zone (Fig. 1). In others they were mainly basal (Fig. 2), and in one the shadows were mainly hilar (Fig. 3). In the remaining cases opacities were seen in more than one zone. In one the opacities presented a honeycombed appearance (Fig. 2) in the right lung, the left lung being emphysematous.

The appearances described above are quite unlike those seen in segmental collapse, bronchial or lobar pneumonia. Although the appearance in Fig. 1 may

FIG. 1.—Bilateral apical opacities.

FIG. 2.—Honeycombed appearance of opacities at base of right lung with emphysema of left lung.

FIG. 3.—Hilar shadows.

be mistaken for bilateral upper lobe collapse, appearances at necropsy were those of atypical pneumonia.

Diagnosis

To a large extent the diagnosis was made by a process of exclusion. It soon became apparent that we were dealing with a type of pneumonia that did not respond to penicillin in the usual dramatic manner. Bronchial breathing and impairment of percussion note were conspicuous by their absence, although dyspnoea was a marked feature in many cases, especially at the onset of the illness. The temperature was remittent and came down gradually by lysis (Figs. 4 and 5). The diagnosis was confirmed by radiology and serologically by noting the presence of cold agglutinins in the serum.

Prognosis

There were four deaths in these nine cases, a higher mortality than in similar series published from other countries. Three deaths were in young infants. The poor nutritional state of our children may have been a deciding factor in the poor prognosis. The severe cases that ended fatally appeared to fall into a clinically related group with high fever, severe cough, marked dyspnoea, cyanosis, sweating and collapse without physical signs of consolidation or radiological evidence of pneumonia.

Treatment

Aureomycin was used in six cases when combined sulphadiazine and penicillin treatment had been found to be ineffective. In three cases the tempera-

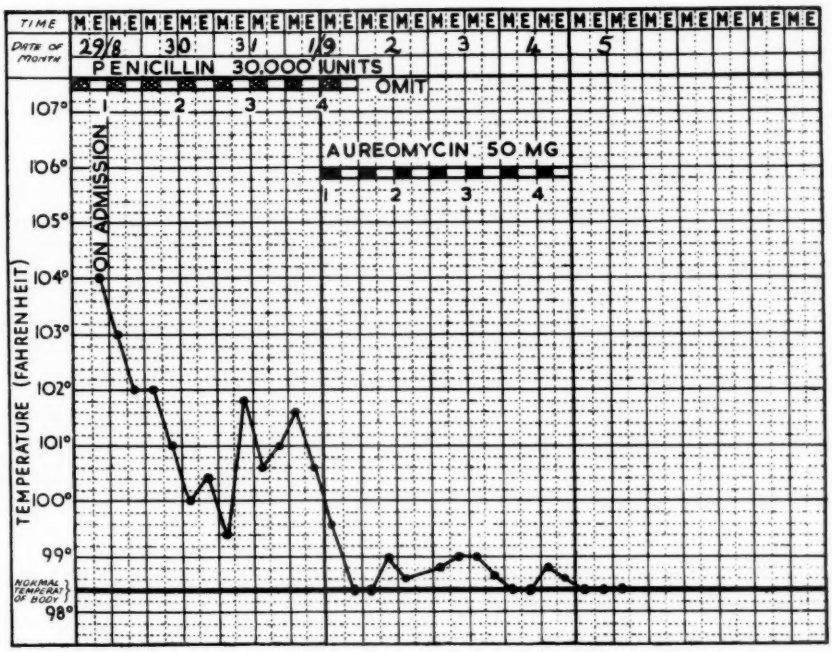


FIG. 4.—Temperature chart showing quick response to aureomycin.

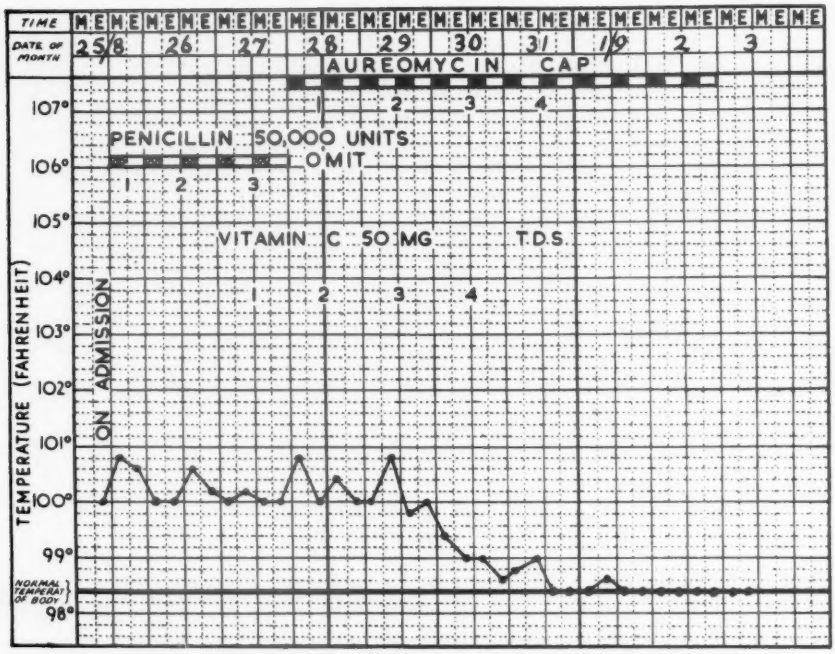


FIG. 5.—Temperature chart showing persistence of low fever in spite of penicillin. Temperature settled down after aureomycin.

ture settled down in 18, 24 and 60 hours respectively, and in two others only after six and 15 days respectively. The last ended fatally in spite of the drug. Three patients, who did not receive aureomycin, also died and in one the temperature settled although penicillin alone had been given, but the child succumbed to an attack of diarrhoea. Aureomycin was thus effective in only a few of our cases.

Pathology

Out of the four deaths permission for a necropsy was obtained in three. In our two earliest cases neither serological nor radiological examinations had been done, as we did not suspect that atypical pneumonias occurred in this country. The necropsy findings were so unlike those of bacterial pneumonia and agreed in every detail with the pathological features of atypical pneumonia described by Golden (1944) that we investigated subsequent cases with considerable care. In the two latter deaths the diagnosis of atypical pneumonia had been made during life on serological and skiagraphic appearances, and confirmatory evidence was obtained at necropsy in one. In the other necropsy was not permitted.

Macroscopic Appearances. Although the pleura (Fig. 6) was smooth and glistening for the most part, the lungs showed focal lesions consisting of slightly raised, whitish areas distributed particularly around bronchi, near which the lung tissue was often haemorrhagic. The smaller bronchi stood out rather prominently and their walls appeared thickened. On squeezing the lung mucopurulent material was extruded from the bronchi.

Microscopic Appearances. The general appearance of a section is shown in Fig. 7. A marked degree of cellular infiltration was seen around the bronchioles, the cells spreading in the interstitial tissue of the lung for some distance. The perivascular spaces were prominent on account of oedema. Several such patches of peribronchial and interstitial cellular infiltration separated by congested and oedematous lung were to be seen in a section. The cells around bronchioles as well as those in the alveolar septa were mononuclear (Figs. 8 and 9). The bronchiolar lumina contained desquamated cells of the mucous membrane and cellular debris. In some bronchioles the entire mucous membrane was desquamated, but

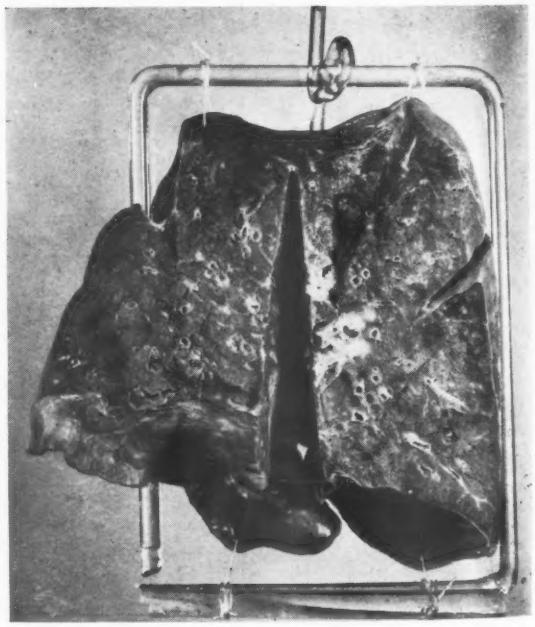
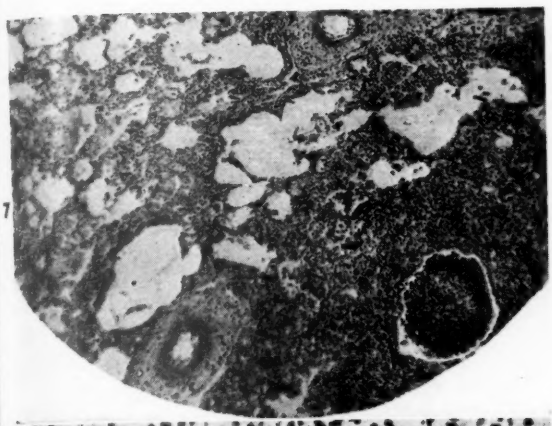
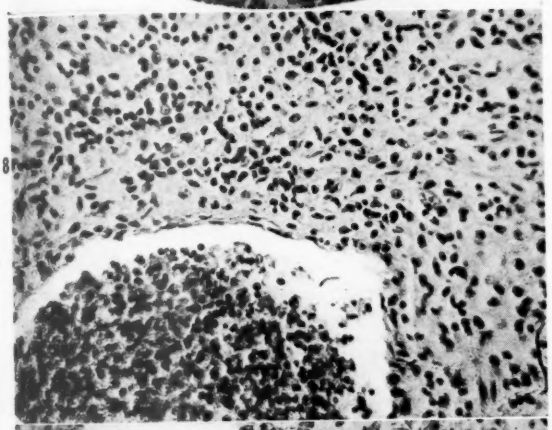
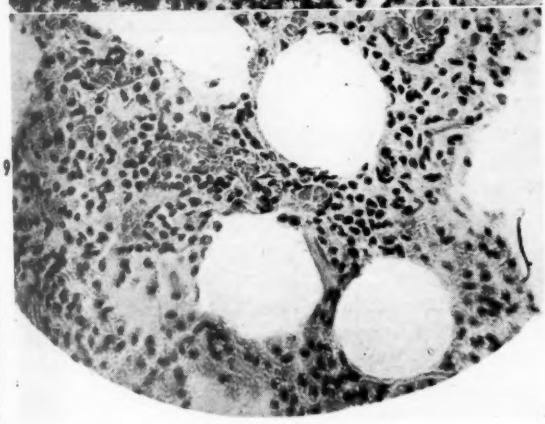
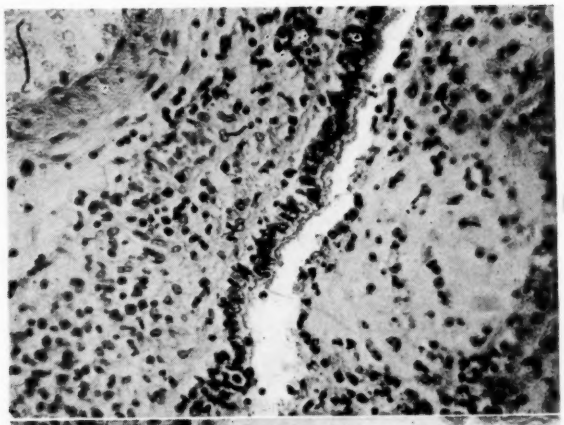


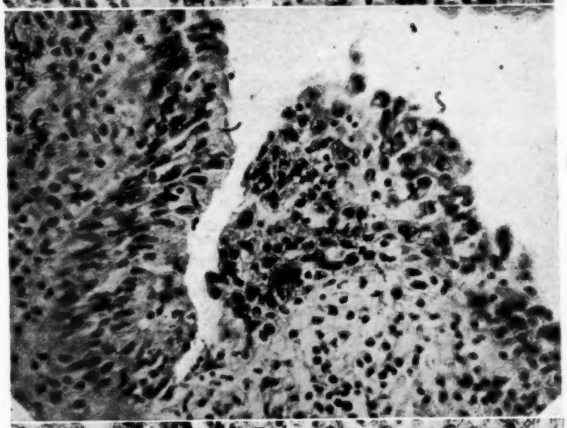
FIG. 6.—Hemisection of lung showing marked prominence of bronchioles due to peribronchiolitis. ×½.











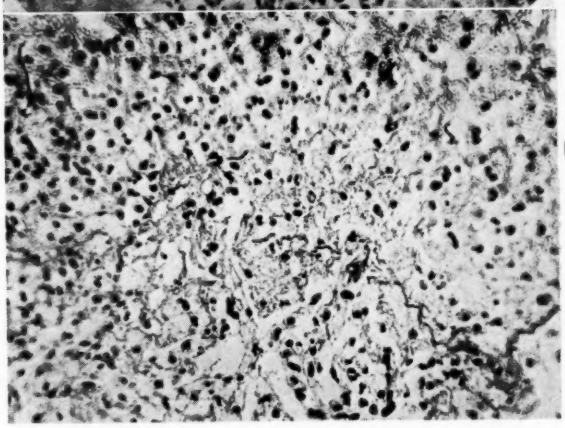


FIG. 7.—Low-power view of section showing a bronchiole containing cellular debris with marked peribronchiolar cell infiltration, and perivascular oedema. Haematoxylin and eosin × 50.

FIG. 8.—High-power view of Fig. 7 showing large numbers of mononuclear cells around a bronchiole the lumen of which contains desquamated cells and cellular debris. Haematoxylin and eosin × 200.

FIG. 9.—High-power view of Fig. 7 showing alveolar septa heavily infiltrated with mononuclear cells. Note prominent capillaries in interstitial tissue and patent alveoli. Haematoxylin and eosin × 200.

FIG. 10.—Intact mucous membrane of a larger bronchiole. Polymorphonuclear leucocytes suspended in mucoid material inside lumen. Mononuclear cell infiltration in the peribronchial tissue. Haematoxylin and eosin × 200.

FIG. 11.—Focus of squamous cell metaplasia. Haematoxylin and eosin × 200.

FIG. 12.—Thread-like appearance of fibrin inside an alveolus. Weigert's fibrin stain × 200.

in others, particularly the larger ones, the mucosa was intact, the lumen being occupied by polymorphonuclear leucocytes suspended in mucoid material (Fig. 10). An occasional bronchiole showed metaplastic transformation of the lining to a squamous type of epithelium (Fig. 11). In contrast to the involvement of alveolar walls, the alveolar lumina contained air (Fig. 9). In some alveoli, however, there was fibrin which either filled the alveolar space or formed a layer on the alveolar wall. More often the fibrin appeared in the form of fine threads forming a network entangled in which were the nuclei of alveolar cells (Fig. 12).

Discussion

We have labelled the series reported here as 'atypical' pneumonias because we are of the opinion that they will probably be found on further investigation to be due to more than one aetiological factor, but clinically, serologically, radiologically and pathologically all of them are quite distinct from bacterial pneumonias.

It has to be decided whether the causative agent in this series is an ill-defined virus such as the one described by Eaton, Meikeljohn, VanHerick and Talbot (1942) as being responsible for the atypical pneumonias or whether it is one of the known infective agents such as the viruses of psittacosis-ornithosis or influenza, or a rickettsia (*R. burneti*). Clinically and radiologically it is impossible to distinguish ornithosis from primary atypical pneumonia, but as the cold agglutination titre was fairly high in a large number of our cases (Morgan and Finland, 1948, have shown that it is usually negative in the former), we think it unlikely that the virus of psittacosis-ornithosis was the causative agent in this series.

Although it may be thought that some of these cases may have been due to the influenza virus, clinically they have not resembled influenzal pneumonia, a condition usually appearing in epidemics and characterized by cyanosis, a very high swinging temperature and a high mortality, and not by a high titre of cold agglutinins.

The evidence against our cases belonging to the Q fever group (*R. burneti*) is that, to our knowledge, Q fever has not been reported in children but only in workers in abattoirs and laboratories and in military personnel. The cold agglutinins are also not increased in Q fever. Recently seven further children with atypical pneumonia have been investigated for agglutinins against *R. burneti*, with negative results.

Skiagraphic evidence and necropsy findings also support the view that we are dealing with atypical pneumonias probably of viral origin. Radiological appearances, similar to those we have described, have been reported by Parker *et. al* (1947) in a carefully investigated series of cases of primary atypical pneumonia. Moreover, the disappearance of the lung opacities in our cases after the administration of aureomycin when penicillin and sulpha drugs were ineffective, suggests that our cases may have been viral in origin. The naked eye appearances of the lungs at necropsy tally with the descriptions and illustration of Golden (1944), and the histological changes agree in every detail with his findings and those of Parker *et al.* (1947).

It is thus seen that our cases bear a close resemblance clinically, radiologically, serologically and pathologically to the primary atypical pneumonias described in other countries, but there are certain doubts about labelling them as such.

In the first place four of our nine patients died. Atypical pneumonia is generally reported as a mild disease with a negligible mortality but in two epidemics in Minneapolis Adams, Green, Evans and Beach (1942) reported a 20% mortality, and it is now widely accepted that primary atypical pneumonia is not entirely harmless in small infants. Three out of the four deaths in our series occurred in infancy. One of these though 14 months of age weighed only 12 lb.; another, aged 4½ years, died within 24 hours of admission.

The second doubt is about our cold agglutination titres. Although Peterson, Ham and Finland (1943) and Turner (1943) suggested that an increase in cold agglutinins was peculiar to primary atypical pneumonia, Viswanathan and Natarajan (1945) have reported similar increases in tropical eosinophilia. However, none of our cases showed an eosinophilia or suffered from such conditions as trypanosomiasis, hepatic cirrhosis, paroxysmal haemoglobinuria or haemolytic anaemia, where too, the cold agglutinins are said to be increased. As Horsfall (1946) claimed that 8·1% of 209 normal subjects showed increased titres of over 1 in 40, we investigated 81 cases at random for cold agglutinins.

Of 16 cases diagnosed as atypical pneumonia radiologically (only six are included in this series), nine (56%) showed a titre of 1 in 64 or over. Of 65 other cases which included eosinophilia, haemolytic anaemias and various types of respiratory infections, e.g. bronchitis, bronchiolitis, bronchopneumonia, bronchiectasis, lung abscess, pulmonary tuberculosis, tuberculous meningitis, diarrhoea, malnutrition, nephritis and congenital heart disease, only three cases (5%) showed a titre of 1 in 64 or over. We have not found it possible to carry out the

other serological test (the streptococcus M.G. titre) which has been used in the diagnosis of atypical pneumonia. However, as this titre is increased in only 30% of the cases, we have considered the cold agglutinin test, which is increased in over 50%, of greater value.

Robertson and Morle (1951) explain what they call the primary atypical pneumonia syndrome as being due to a segmental aspiration pneumonia. They doubt its viral origin and are of the opinion that it results from aspiration of products from an associated upper respiratory tract infection. They conclude: 'Our experience with this series of cases has led us to believe that the name and diagnosis "primary atypical pneumonia" is meaningless, as it is not a specific condition but merely represents a segmental aspiration pneumonia'. The evidence presented in this paper, particularly the skiagraphic appearances and the necropsy findings of a definite interstitial type of pneumonia with patent alveoli, is definitely against this condition being a segmental aspiration pneumonia. While we are willing to admit that some of the cases, particularly the milder ones in which penicillin appeared to be effective, may be examples of aspiration pneumonia, we cannot agree that all are of this nature.

Summary

The paper deals with nine cases, including four deaths, of atypical pneumonia occurring in Ceylonese children. The clinical features, laboratory findings, radiological appearances, treatment and pathological findings are described, and it is concluded that the illness, although not necessarily of uniform origin, differs from bacterial pneumonia, ornithosis, influenza and Q fever.

We thank Professor W. A. E. Karunaratne, Professor of Pathology, University of Ceylon, for facilities, Dr. O. C. Raffel for general assistance, Messrs. K. M. M. Michael and P. Le Motte for the photographs, and Messrs. Justin de Silva, P. D. S. Amerasekera, G. A. H. Jayaweera and J. Fernando for technical assistance.

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RECURRENT PAROTITIS IN CHILDREN

BY

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From time to time a child is seen with swelling of the parotid gland in whom mumps is diagnosed, yet the parent states that the patient has had that disease several times before. Due largely to the work of Payne (1933, 1938, 1940) the condition of recurrent parotid swelling has been defined as a clinical entity, but most of the published accounts refer to adults. The disease, however, is by no means rare in children, as can be seen from the fact that 17 examples have been seen in one part of the Midlands in the past five years. The salient features of these patients are recorded in the table.

The essential feature of the condition is swelling of one or both parotid salivary glands. This recurs once or many times (Fig. 1). Sometimes the swelling is confined to one side, but recurrences need not always affect the same side and both sides may be involved on each occasion; or a unilateral case may become bilateral or vice versa. In the examples recorded here the whole parotid gland has been enlarged and there was usually tenderness, but there has been no redness or oedema of the overlying skin.

FIG. 1.—Right-sided parotitis.

In frequently recurring cases not only does the enlargement tend to be greater than in those which relapse rarely, but enlargement of varying degree may persist between periods of activity.

Pain has been a variable feature: probably some discomfort is always experienced and this may rarely be severe. Usually the sufferers complain of moderate discomfort for the duration of the swelling, which has lasted from a few minutes, especially after treatment, to several weeks.

The onset has usually been abrupt and has in less than a quarter of the patients coincided with the taking of food, although one boy, before he was treated, could always provoke an attack by taking vinegar. The frequency of attacks has varied from about one a year to one a week.

The orifice of Stenson's duct has not appeared abnormal, though Bigler (1946) has described redness and oedema, but no thickening of the duct has been felt.

When the disease was active mucopurulent saliva could nearly always be expressed from the affected gland. In the majority only a small quantity was obtained, but in those children from whose saliva the pneumococcus was isolated a larger amount appeared and in two on several occasions purulent discharge was seen to drip from the orifice of the parotid duct. In most of the patients the secretion presented the 'snowstorm' effect described by Payne (1938), the flakes being small masses of mucus and cells suspended in mucopurulent saliva. After treatment the 'snowstorm' appearance was infrequently seen and between periods of activity little or no discharge could be expressed.

Fever and leucocytosis have been inconstant features. The temperature was often normal at the height of the swelling. The maximum white cell count has been 24,800 per c.mm. with 78% polymorphonuclear cells in a case from which both the haemolytic streptococci and pneumococci were isolated. As a rule the white count has been from 8 to 10,000 leucocytes per c.mm. The usually more severe pneumococcal cases have tended to be associated with the most marked leucocytosis.

The diagnosis is confirmed by sialography, which showed characteristic changes in 13 of the 14 cases in which it was done. This is in contrast to the findings of Bigler (1946) who recorded normal radiographs in the few cases of his series in which this examination was performed.

In each case a plain film was taken to exclude the presence of a calculus which was never found. Next, following the technique of Payne (1931) and

Ollerenshaw and Rose (1951) 1-2 ml. of 'neohydriol fluid' was injected with a syringe and small blunted hypodermic needle into Stenson's duct and lateral and postero-anterior projections were made. In the normal gland the ducts were well outlined and it

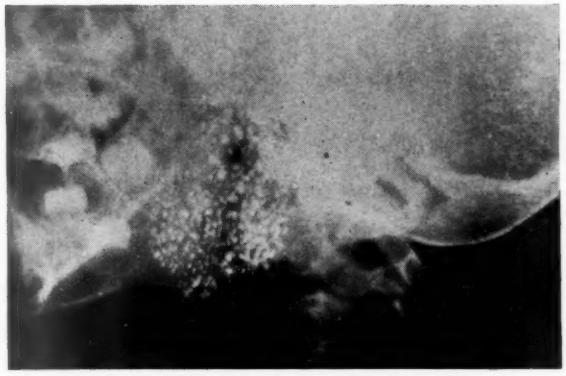

FIG. 2.—Sialogram showing mild sialectasis.

proved impossible to avoid some filling of the acini. This acinar filling, called by Samuel (1950) 'sialo-acinar reflux', has been shown by Ollerenshaw and Rose (1951) to be the normal result of proper filling with the opaque medium. In 10 patients of this series a spherical dilatation of the finer ducts was seen: in one case infected with the pneumococcus, a gross type of change, described by Payne (1933) as destructive, was seen, and in two of the remaining three the dilatation was intermediate between the two types (Figs. 2, 3 and 4). In one only was the sialogram normal. In addition, the main ducts in four children showed some dilatation with a tendency to beading.

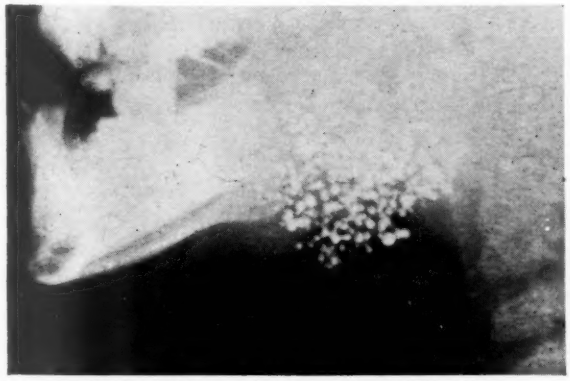

FIG. 3.—Sialogram showing moderate sialectasis.

An interesting feature was the persistence of small quantities of opaque medium in the glands of three patients in whom radiography was repeated after intervals of six months, 13 months and two years after the first examination.

Bacteriology

Three types of purulent parotitis are described by Payne (1940): first that due to *Staphylococcus aureus* which gives rise to acute parotitis; secondly that caused by the α-haemolytic streptococcus which results in recurrent parotitis; and thirdly that from which the pneumococcus has been isolated, a recurrent parotitis of a more severe type which may proceed to abscess formation. Acute parotitis is not included in this paper, as no example of this condition has been seen which went on to the recurrent form of the disease.

The majority of the cases in this series, all but five, fall into the second group and the α-haemolytic streptococcus was isolated from the parotid saliva in each of these. In the remaining five pneumococci in pure culture were isolated in two and both pneumococci and α-haemolytic streptococci were obtained from the other three. Three of the latter

FIG. 4.—Sialogram showing severe sialectasis.

five were the most severe examples in the series and one child had severe pain and constant swelling of both parotids. Unfortunately full investigation and treatment were refused and he could not be traced. Yet not all cases associated with the pneumococcus are necessarily severe, as the only normal sialogram seen was that of a boy from whose parotid secretion pneumococci and α-haemolytic streptococci were isolated.

Treatment

Effective treatment can hardly be expected without an understanding of the cause of the condition. Possible factors concerned in the aetiology are discussed below, but it would seem most important to eliminate septic foci in the mouth, particularly carious teeth and infected tonsils, and this was done when considered necessary. It is perhaps significant that the only normal sialogram was obtained from a patient in whom no evidence of infection was found.

TABLE

SALIENT FEATURES OF 17 CASES OF PAROTITIS

Name	Sex	Age when First Seen (years)	Age at Onset (years)	Side Affected	Frequency of Attacks	Duration of Attacks	Symptoms	Organism	Sialogram	Septic Foci	Treatment	Result of Treatment
D.A.	M	11	9	R	2 a year	2 weeks	Marked pain. Unable to chew	αHaemolytic streptococcus	Mild sialectasis	Otitis media, tonsillectomy (5) turbinectomy (8), dental caries†	One course penicillin	No relapse for 3 years
B.D.	M	10	9½	R > L	5 in 6 months	3 days	Marked pain, unable to chew, vinegar provokes	αHaemolytic streptococcus	Mild sialectasis	Recurrent aphthous stomatitis, recurrent tonsillitis	One course penicillin	Improved. Attacks last ½ hour with only slight discomfort. Three in fourth year after treatment
K.J.	F	3	2½	R	3 in 6 months	Up to 4 weeks	Painful	αHaemolytic streptococcus	Mild sialectasis	Dental caries, otitis media	One course penicillin	Greatly improved. One ½ hour attack in 4 years
S.S.	M	11	Unknow *	R	Frequent	Several days	Slight pain	αHaemolytic streptococcus	Mild sialectasis	Ectodermal dysplasia, recurrent tonsillitis	One course penicillin	Greatly improved. Three attacks of 1 day each in 3 years
C.S.	M	13	Unknown*	R	Frequent	Several days	Slight pain	αHaemolytic streptococcus	Not done	Ectodermal dysplasia, recurrent tonsillitis	Massage only	Improved. Attacks fewer and last up to 3 days
D.M.	M	5	4	R	4 a year	1-3 days	Slight discomfort	αHaemolytic streptococcus	Unsuccessful	Dental caries	Massage and one course parenteral penicillin	No attack in 6 months
E.F.	M	13	3	R & L	2-3 a year	2 weeks	Slight discomfort	αHaemolytic streptococcus Pneumococcus	Normal	None	One course penicillin, one course streptomycin	Slight improvement after first course. Then organisms became penicillin resistant. After second course attacks lasted 1-2 days. Incidence unchanged
T.L.	M	5	5	L > R	2 in a month	3 days	Slight discomfort	αHaemolytic streptococcus	Mild sialectasis	Otitis media, recurrent tonsillitis	Massage only	Much improved. One attack in 3 years
O.M.	F	4½	2½	L > R	1 a month	Up to 7 days	Marked pain, drinks only cold fluids	αHaemolytic streptococcus Pneumococcus	Moderate sialectasis	Dental caries, recurrent tonsillitis	Two courses penicillin	Much improved. Two mild attacks in 18 months after second course
B.K.	M	9	7	R	6 a year	1-7 days	Painful	αHaemolytic streptococcus	Mild sialectasis	Recurrent tonsillitis, tonsillectomy & antrostomy (9)	One course penicillin	No relapse for 3 years
J.F.	F	2	1 1/12	L > R	1 a month	Up to 7 days	Slight discomfort	αHaemolytic streptococcus	Mild sialectasis	Dental caries, tonsillitis	One course penicillin	Greatly improved. One mild attack in 4 years
J.T.	F	4	3¾	R & L	2 in 3 months	6 weeks	Slight pain, siallorrhoea	Pneumococcus	Marked sialectasis	Otitis media, tonsillitis, tonsillectomy (5)	Two courses penicillin	Slight improvement after first course. Two attacks in 18 months after second course
R.F.	M	11	6	R & L	Almost continuous	—	Severe pain, constitutional upset	Pneumococcus	Not done	Dental caries	None	Not traced
M.H.	F	3½	1½	R	1 a year	3 weeks	Slight pain	αHaemolytic streptococcus	Moderate sialectasis	Dental caries	One course penicillin	One attack lasting 6 days in 7 months
A.H.	F	8	7	R & L	2 a year	3 days	Slight discomfort	αHaemolytic streptococcus	Mild sialectasis	Dental caries	One course penicillin	One attack in 3 years
L.T.	M	11	2½	L	4 a year	2-14 days	Painful	αHaemolytic streptococcus	Mild sialectasis	Recurrent tonsillitis, tonsillectomy (8)	One course penicillin	No attack in 3½ years
R.H.	F	12	11	L > R	9 in 1 year	3 days	Slight discomfort	αHaemolytic streptococcus Pneumococci	Mild sialectasis	Tonsillitis preceded each attack	One course penicillin	Insufficient time for assessment

* Orphan brothers from whom no accurate history could be obtained. †Numbers in brackets indicate age at which operation was performed.

The dilatation of the finer ducts seen in the sialograms suggests that stagnation of secretion favours the development of infection. Clearly such stagnation should be prevented, and this is best done by massage, a method strongly advocated by Payne (1933). The patients, or their mothers in the case of the youngest, were instructed to massage the cheek overlying the gland from the periphery of that structure towards the duct orifice. The effect of this simple procedure was difficult to assess but it was undoubtedly useful and sometimes seemed to abort attacks.

In 1948 an attempt was made to attack the infecting organisms directly by injecting penicillin into Stenson's duct. This method was used independently by Rose (1950) with 'uniformly satisfactory results', but no details were given in his article. Penicillin, 100,000 units per ml., was injected slowly into the orifice of Stenson's duct by means of a syringe and blunt-pointed needle. Usually 1 ml. was slowly injected into the gland and no anaesthetic was found necessary even in quite small children, for with gentleness the injection appeared to cause little discomfort. The treatment was repeated daily for about six days, and in some cases a second course was given after an interval of some months. On one occasion streptomycin was substituted for penicillin as the infective organism had become resistant to penicillin. The results achieved by this treatment have been encouraging but many patients must be followed well into adult life before its true worth becomes apparent. Some improvement, over and above that caused by simple massage, always followed and in some instances the results were striking; three patients have had no relapse for over three years after one course of injections and three others have experienced but one attack in the same period (four years in two cases). Improvement generally took the form of a reduction in the duration of the periods of activity and most of the children stated that their relapses lasted for a much shorter period and caused less discomfort.

It is probably true that dilatation of the parotid duct *per se* is a valuable element in treatment, making drainage assisted by massage easier. The preliminary sialogram often caused an unexpectedly long period of freedom from activity (three years in one child) yet the persistence of opaque material in the gland for periods up to two years shows that massage does not always result in complete drainage.

Parenteral injection of penicillin, 100,000 units every six hours for five days, has not proved effective in stopping relapses, though Debré and Loewe-Lyon (1951), in a girl of 8 years, found that large doses of penicillin given parenterally cut short the relapses. In this case 150,000 units a day proved ineffective while 800,000 units or more daily were successful.

A further difficulty in assessing the results of treatment is shown by two of the children's mothers who both had the disease in girlhood and in whom spontaneous cure took place.

Discussion

Why should the parotid gland alone of the salivary glands be affected by this disease? Consideration of the structure of the glands may supply an answer. All three pairs of salivary glands are formed of lobules consisting of acini drained by small ducts. The structure of these acini varies according to whether they secrete mucus or serous material. Submaxillary and sublingual salivary glands are 'mixed' and contain both mucous and serous acini but the parotids are purely serous. Mucous acini are comparatively large and joined to the ducts by wide channels, while serous acini are smaller and have longer and narrower connecting channels, an arrangement which favours stagnation of secretion (Sharpey-Schafer, 1949). Moreover, Stenson's duct is about 2 inches long, with a diameter of $\frac{1}{8}$ inch, though the terminal opening is even narrower and the duct is angled as it traverses the buccinator muscle. Similarity to bronchiectasis developing in a portion of lung collapsed as a result of obstruction of the segmental bronchus is apparent and the importance of adequate drainage seen. In fact immediate improvement has been seen when a free flow of parotid saliva has been effected. If, as seems likely, infection ascends up the duct from the mouth, the importance of any buccal focus of infection is clear and in the majority of patients dental infection, septic tonsils or obstruction of the nasal airway has been noted. This assumption is suggested by the findings of Berndt, Buck and Buxton (1931) who injected the parotid ducts of 15 dogs with a suspension of *Staphylococcus aureus* and produced parotitis in 10 of them, while similar injection into the artery of the parotid caused parotitis in only three of 15 animals. A further point is that if anything should interfere with adequate chewing stagnation of saliva in Stenson's duct may occur, and Payne (1940) remarks that many patients date the origin of their symptoms to the time of the first or second dentitions. He also points out that mucus is bactericidal and that the parotid is primarily a serous gland. In this connexion two of the present group of patients are interesting. These two are orphan brothers and both suffer from congenital ectodermal dysplasia. Their mouths are rather dry and presumably scanty parotid secretion favours stagnation and resulting ascending infection.

Bruce Pearson (1935) described 11 cases, seven under 12 years of age, of recurring parotid swelling characterized by a lack of evidence of infection and commonly a history of allergy. During an attack of swelling in one of these cases plugs containing eosinophils were obtained from Stenson's duct. He postulated that the condition resulted either from obstruction to Stenson's duct by spasm or oedema or else to achalasia of the duct. In three of the present series there was a family history of allergy; in one the mother was asthmatic, in the second an aunt had hay fever and in the third an aunt suffered from asthma. Two of the children's mothers had suffered from a similar disease, in one case until the age of 14 and in the other from 8 to 11 years of age, although in neither of these families was any form of allergy detected. One boy had paroxysmal rhinorrhoea with an eosinophil count of 8% without any allergic family history, but he was the only patient in whom any form of allergy was detected. In no case were eosinophil cells found in the parotid secretion. In view of the frequency of allergy in one form or another in the general population there seems insufficient evidence that it played a causative role in these 17 patients.

Differential Diagnosis. The commonest initial diagnoses made in these children were either mumps or cervical adenitis. The latter is soon refuted by careful examination. One attack of mumps is generally regarded as conferring a permanent immunity and a history of contact has not been obtained in a single case. In mumps the typical mucopurulent secretion cannot be obtained from Stenson's duct. Applebaum (1944) has shown that the serum amylase is raised above the normal value of up to 150 units in 95% of mumps cases during the active phase of the disease and in three of this series a normal value was obtained at the height of the parotid swelling.

Neoplasms, leukaemia, sarcoidosis and salivary calculus are rare courses of parotid enlargement in children and are normally readily excluded.

Summary

Seventeen cases of recurrent swelling of the parotid gland are described.

The condition is thought to be due to infection originating in the mouth or post-nasal space ascending to the parotid duct, associated with stagnation of the secretion in the gland.

A method of treatment is described, which commonly cut short the period of activity of the disease and sometimes caused complete relief.

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Addendum

During the preparation of this paper a further three children suffering from the same condition were seen. Two were bilaterally affected and both of these harboured α-haemolytic streptococci and pneumococci, while from the other α-haemolytic streptococci alone were isolated. One course of local penicillin in all three has resulted in four months' freedom from relapse.

PULMONARY THROMBOSIS AND ITS ASSOCIATION WITH UNEXPECTED DEATH IN CHILDHOOD

BY

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Thrombosis of pulmonary vessels unassociated with local sepsis or cardiac deformity is rarely recognized in infancy and childhood. The condition is not usually considered by clinicians or by pathologists doing necropsies in this age period, and I have been unable to find a paper discussing this subject in the available literature.

This communication is concerned with pulmonary vascular thrombosis in 15 children seen in a series of approximately 200 consecutive necropsies.

Material and Methods

The material consisted of routine necropsies at two children's hospitals, and also cases referred through the Coroner.

A particular necropsy method was used, not for the purpose of finding vascular thrombi but in an attempt to leave fluids and inflammatory exudates in the respiratory passages in their natural position so that their distribution could be studied later in sections. In most instances the trachea was tied with a cord or clamped with artery forceps before opening the body cavities. The heart and lungs were removed together from the body, and the lungs were not handled with the fingers or compressed. The cavities of the heart were opened for general inspection. The lungs and the heart were then placed under cotton wool in fixing fluid, and the lungs cut after fixing from 36 to 48 hours. Blocks for histology were taken from the lungs as far as possible at right angles to the direction of the bronchi, and treated by routine methods.

Cases were only included when no sepsis was found in the lungs. Thrombosis was recognized on histological criteria only and cases in which the thrombi were not certainly ante-mortem in type were recorded as negative. Cases with congenital deformity of the heart were not examined for thrombi and thus these were automatically excluded from the series.

The 15 cases fell into four distinct clinical groups: I, in the neonatal period (two cases); II, terminal incidents in children with chronic disease (four cases); III, children admitted to hospital with acute severe illness (five cases); IV, children who had been referred to the Coroner on account of their death being unexpected (four cases).

Since these groups present different problems the cases will be presented and discussed in these groups.

1. Neonatal Period

Case (a). Aged 5½ days, an immature child (birth weight 4 lb. 14 oz.) when 24 hours old had shown signs of cerebral irritation, and at 4 days was thought to be spastic. He had no cough. In the terminal two days sclerema developed associated with a subnormal temperature. At necropsy, ante-mortem thrombosis was present in the lungs with small zones of fresh haemorrhage from alveoli. Thrombosis was also present in the larger cerebral vessels, choroid plexus and renal veins. The larger thrombi in the lung appeared histologically to be of the same age as those in the renal vessels.

Case (b). This was a premature infant aged 9 days. Cyanotic attacks began when he was aged 5 days. There was a sudden rise in temperature to 101° F. 18 hours before death. For a few hours before this the child had passed loose stools and vomited (see Fig. 1). A clinical diagnosis of respiratory failure or aspiration of vomit was made. At necropsy, certain organs were seen to be immature. Thrombi were present in cerebral vessels and the brain showed kernikterus. Thrombi were present in the lung, and there was also a small amount of oedema in the alveoli.

Both of these children were initially extremely 'weakly' but in both the immediate factor in death seemed to be generalized vascular thrombosis in which the lung vessels played a minor part in the first case, but probably the major part in the second. Thrombosis of the choroid plexuses and cerebral vessels is well known in the neonatal period (Craig, 1938). The only reported case I have found with associated pulmonary thrombosis is that recorded by Cruickshank (1930) who found thrombosis of pulmonary vessels in one case among 30 cases showing

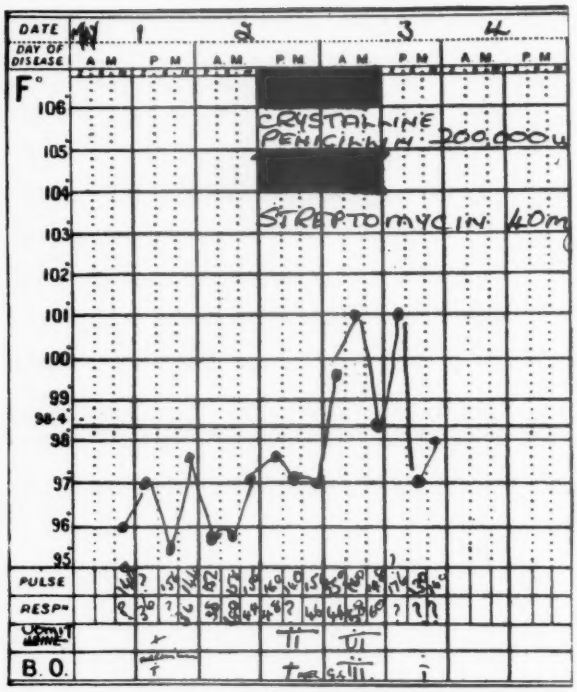

FIG. 1.—Photograph of the temperature chart of Case Ib showing pyrexia and the incidence of vomiting and diarrhoea.

venous thrombosis elsewhere in a series of 800 neonatal deaths. We have no direct clue as to the cause of the thrombosis in the first case. In the second case the vomiting and frequent stools suggested an associated blood fluid disturbance. In the first case the sclerema was probably related to circulatory inadequacy and in both cases circulatory failure probably preceded the thrombosis.

II. Terminal Incidents after Wasting and Long-standing Sepsis

Case (a). Aged 10 months, this child had a gangrenous intussusception at the age of 8 months. Wound sepsis followed with a fistula and chronic sepsis. The child continued in a debilitated state for two months. Three days before death there was a rise in temperature and respiration rate, and cyanosis (Fig. 2). This persisted with no response to penicillin and streptomycin. The clinical diagnosis was pneumonia. Before the pyrexia the child had passed loose stools and a greater number of loose stools were passed on the first day of pyrexia. At necropsy, chronic peritonitis was present with a few loculations of pus. There was recent thrombosis of the inferior vena cava and pelvic veins. In the lung there was thrombosis of many vessels and a small amount of oedema.

Case (b). A boy aged 3 years had been ill for three months with persistent vomiting and considerable wasting. There was necrosis of the gums and finger nails and also desquamation of the skin, particularly of the hands and feet. The clinical diagnosis was acrodynia. Two hours before death there was a sudden onset of dyspnoea with moist sounds in the chest. The temperature was not raised. At necropsy, there was thrombosis in the inferior vena cava and also in some hepatic veins. In the lung there was extensive thrombosis throughout all the major vessels, both arteries and veins, and some alveolar oedema. The thrombi in the lung did not appear to be more recent than those in the inferior vena cava or hepatic veins.

Case (c). Aged 5 months, this child had shown mental retardation from birth. At the age of 3 months he presented with increasing jaundice and a laparotomy was performed. He was finally admitted with a history that pus had been discharging for two days from the abdominal wound. Two days before death the temperature suddenly rose. This was associated with the bowels being opened three times a day (Fig. 3). The clinical diagnosis was septicaemia. At necropsy, the underlying disease was chronic hepatitis with extensive liver damage and fibrosis. In the lung many vessels were thrombosed and there was some alveolar oedema.

Case (d). This child aged 8 weeks was prematurely born of a mother with syphilis. He was admitted to hospital with a generalized rash of specific pemphigus and with rhagades, sore buttocks and a history of snuffles and nasal discharge from birth. There had been recent epistaxes. Although ill, the child's condition did not cause acute concern. He unexpectedly collapsed and died within 15 minutes of the onset of stertorous breathing. At necropsy, multiple miliary gummata of the liver were present. Spirochaetes were demonstrated in the liver and adrenal glands. There were recent antemortem thrombi in vessels of the kidneys and in the main

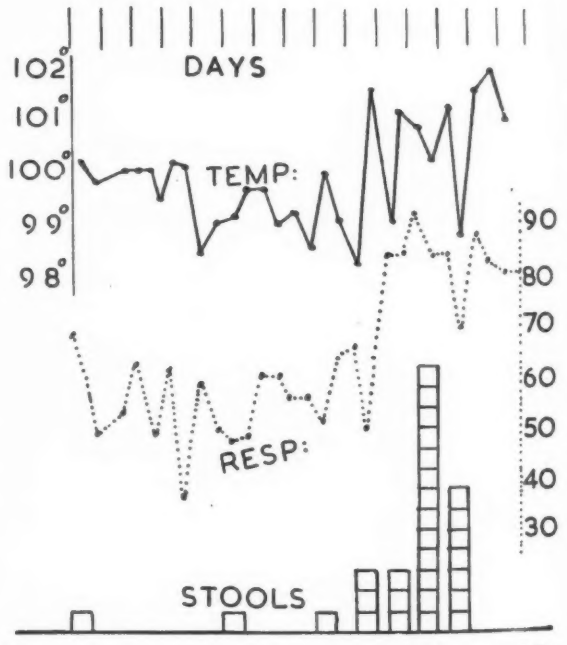

FIG. 2.—Diagram of the temperature and respiration rate of Case IIa showing also the number of stools passed.

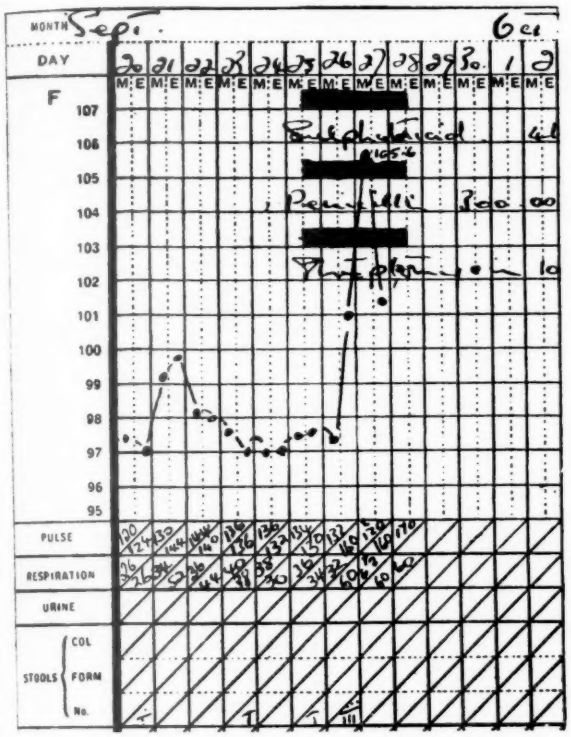

FIG. 3.—Photograph of the temperature chart in Case IIc.

pulmonary veins. There was a small amount of alveolar oedema. No evidence of inhalation was found.

These children were all severely ill with different diseases and venous thrombosis appeared to be the precipitating terminal incident. In two cases (b) and (d) death was very rapid with symptoms similar to those of inhalation of regurgitated stomach contents or acute left heart failure. The other two cases presented a definite clinical picture with a raised temperature and respiratory rate showing no response to chemotherapy or antibiotics.

A rise in temperature was described by Bailey and Hass (1937) in association with cerebral sinus thrombosis in infants. This rise in temperature was well recognized in the older literature in adults. Möller (1922) in an extensive review of pulmonary thrombosis in adults describes the 'Michaelis' symptom which consists of a marked rise in temperature for no apparent reason—a symptom indicating hidden venous thrombosis.

The rise in temperature and onset of symptoms in cases (a) and (c) seem to be directly related to an increase in the number of stools, reflecting an increase in fluid output. In each case the change in stools preceded the pyrexia by only a few hours. While we have no measurements of blood viscosity in these cases the concentration of the erythrocytes in the blood vessels throughout the body suggested a diminution in the fluid compartment of the blood. This was not seen in the other two cases and we have no clue as to the cause of the thrombosis. The only case I have seen recorded was by Ribadeau-Dumas and Chabrun (1927) who describe the necropsy finding of pulmonary venous thrombosis in a 5-month-old child ill with pneumococcal meningitis; in their case lung infection was also present.

III. Cases Admitted to Hospital with Acute Severe Illness

Case (a). A premature infant, aged 10 months on admission, had retrolental fibro-dysplasia. The child had been 'unwell' for two and a half days. Two to three hours before death he began vomiting with convulsions. The child died almost as soon as he reached hospital and no temperature was recorded. At necropsy, there was thrombosis of the longitudinal sinus, cerebral vessels and parts of the choroid plexus, and in large vessels of the lung. There was some oedema in the alveoli. The connective tissue of the body suggested general dehydration.

Case (b). A baby aged 8 months had a history of a 'cold' for three weeks. The child was admitted with a history of convulsions for one day. On examination there were crepitations in the chest and meningismus. The child died almost immediately upon admission. At necropsy no basic disease was found other than upper respiratory infection. There was thrombosis of cerebral sinuses, part of the choroid plexus and many vessels in the lung.

Case (c). A girl aged 16 months had had an attack of what was diagnosed as 'asthma' two months previously, and was admitted with acute respiratory symptoms suggesting asthma, but no respiratory wheeze was heard on auscultation. The temperature rose to 104° F. The child died within 48 hours of the acute symptoms. The clinical diagnosis was acute laryngo-tracheo-bronchitis. There had been no diarrhoea or vomiting. At necropsy, no gross lesions were found outside the lung. The lung, in addition to thrombosis, showed acute laryngo-tracheo-bronchitis of the exudative type and vascular thrombosis. There was some oedema in the alveoli. No thrombi were found in other organs.

Case (d). Aged 3 months, this child had had no previous illness. He had been 'off' his food for nine days. On the day before admission grunting respirations began with pulse 164 and temperature 100·5° F. On admission the child had a distended, rigid abdomen and died while under operation within 48 hours of the onset of the symptoms. At necropsy, there was acute generalized peritonitis from rupture of a retro-umbilical abscess which had probably arisen in a urachal cyst. Thrombosis was present in cerebral vessels as well as in the lung. There was a small amount of oedema in the lung.

Case (e). A child aged 7 months had had no previous illnesses, but had had a slight cough for three days, had vomited occasionally for two days, and had loose stools on the day before admission. Severe symptoms lasted 12 hours only, and consisted of laboured breathing, temperature 103° F. and a great increase in pulse rate. The child

was admitted as a case of acute bronchopneumonia and died almost immediately. At necropsy, no underlying disease was found other than mild acute upper respiratory infection. There was extensive thrombosis throughout most of the veins of the lung.

In two of these cases (a and b) the clinical picture was complicated by thrombosis occurring in the cerebral as well as in the pulmonary vessels. In one case (d) the pulmonary thrombosis was immediately related to acute peritonitis. In this case, without careful study, the death would have been ascribed to 'operative shock'. In the other two cases the pulmonary thrombosis occurred alone, and was apparently a major factor in death. The necropsy diagnosis without a complete histological study would have been acute bronchopneumonia.

In these cases the history of vomiting or diarrhoea seen in the previous group is also present. Whether a more complete history would reveal further symptoms it is not possible to say, but the experience that has been gained by 'triple' histories taken in coroner's cases suggests that the history obtained in acute diseases is often quite misleading.

IV. Sudden Deaths Referred to the Coroner

Case (a). An immature infant (birth weight 4 lb. 2 oz.) aged 3 weeks was referred to the Coroner as a sudden death. Later a history of loose stools for one day was obtained. At necropsy, the child appeared to be dehydrated. Thrombosis of both pulmonary and cerebral vessels was present, also a small amount of oedema of the lung.

Case (b). The child, aged 4 weeks, was found dead in his cot. He had had a 'cold' for three days and had been off his food for three days. At necropsy, there was massive thrombosis of pulmonary veins and also of small veins of the kidney, and some oedema of the lung.

Case (c). A child aged 7 weeks, was found dead in his cot. He had had a 'sticky' eye for one week before death. At necropsy, no underlying disease was found. Thrombosis of pulmonary, renal and cerebral veins was present.

Case (d). An infant aged 6 months was found dead in his cot. There was a history of diarrhoea for one day. The child was reputed to be teething. At necropsy, the only abnormality found was thrombosis in pulmonary vessels and a small amount of oedema of the lung.

Unexpected deaths in children form one of the most disconcerting problems in paediatric pathology. Since the decline in popularity of 'status thymaticus' the most popular finding has been that of microscopic evidence of upper respiratory infection. Such microscopic inflammatory foci were present in the cases listed above, but in no greater degree than is seen in other children with otherwise adequate causes of death. The history of digestive upset in three of the cases was not obtained at the time of the necropsy but several days later by the hospital almoner visiting the children's homes when the alarm of the sudden death and inquest had subsided.

Discussion

Thrombosis of renal vessels associated with diarrhoea in infancy has been recognized since 1837 (Raynor), and by 1877 (Hutinel) 42 cases had been reported. Thrombosis of the choroid plexus (Craig, 1938) and of the cerebral sinuses, designated 'marantic thrombosis' by Virchow, is similarly well known, but thrombosis of the vessels of the lung in childhood seems to have been overlooked. The cause of this is probably technical as cerebral sinuses and renal veins are obvious at necropsy and changes in colour of the brain and kidney call for elucidation. The pulmonary vessels on the other hand are not so visible, and congestion and consolidation of the lung is so linked with the idea of pneumonia that detailed study of the content of the pulmonary vessels is generally overlooked. Until the post-mortem technique of routine fixing of the lungs with the heart was instituted we did not see pulmonary thrombi. Most lung sections give a false idea of the vascularity of the normal lung. It is surprising how few of the larger vessels contain blood in routine sections of the lung.

Belt (1934) points out that pulmonary thrombosis is found in about 10% of adult medical necropsies and is frequently not associated with embolism. Spain and Moses (1946) found pulmonary thrombosis in 109 of 1,000 necropsies in persons over the age of 20. Brenner (1935) in an extensive study of pulmonary vascular disease, remarks 'It is clear that thromboses are commonly present at autopsy but that only careful search will reveal them in many cases'.

Thrombosis is also known to occur in adults in the presence of lung infection and diseases such as silicosis (Geever, 1947) and tuberculosis (Jones, Black and Sparr, 1950) and may itself produce the terminal incident in these diseases. The child reported by Ribadeau-Dumas and Chabrun (1927) would seem to belong to this group. Eppinger and Wagner (1920) describe pulmonary venous thrombosis in adults associated with primary pulmonary sclerosis. They illustrate a small vessel with extensive intimal proliferation such as was seen in a single vessel in one case in the present series.

The rise in temperature seen in many of the cases in groups I and II seems to be associated with vascular thrombosis irrespective of the site or cause of the thrombosis. In infants it has been observed with cerebral sinus thrombosis (Bailey and Hass,

FIG. 4

FIG. 5

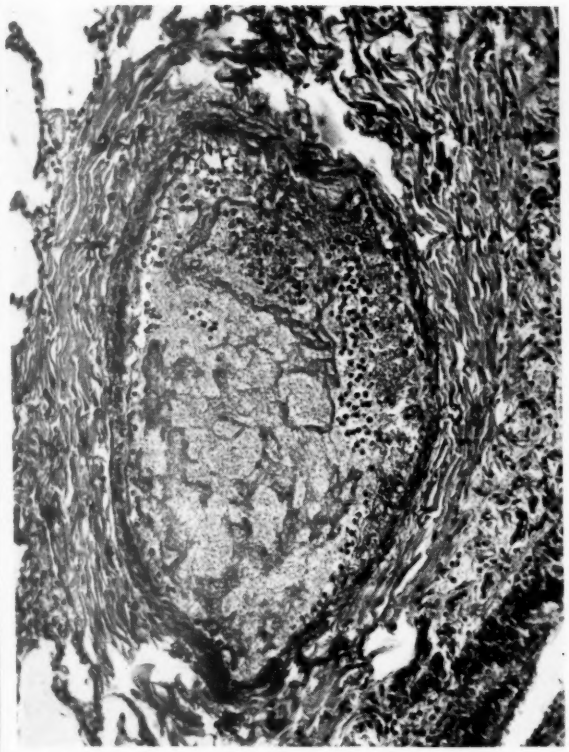

FIG. 4.—Ante-mortem thrombus in a small vein. Masson trichrome ×110.

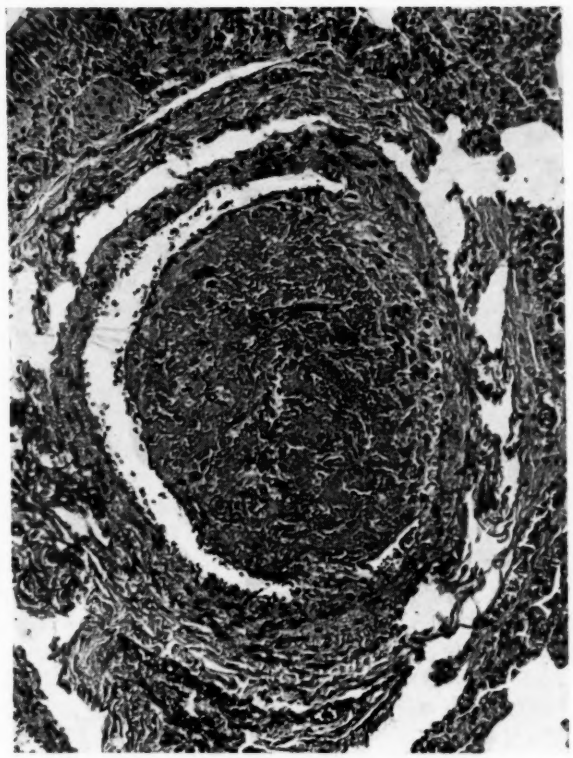

FIG. 6.—Thrombus in a small artery. Masson trichrome ×100.

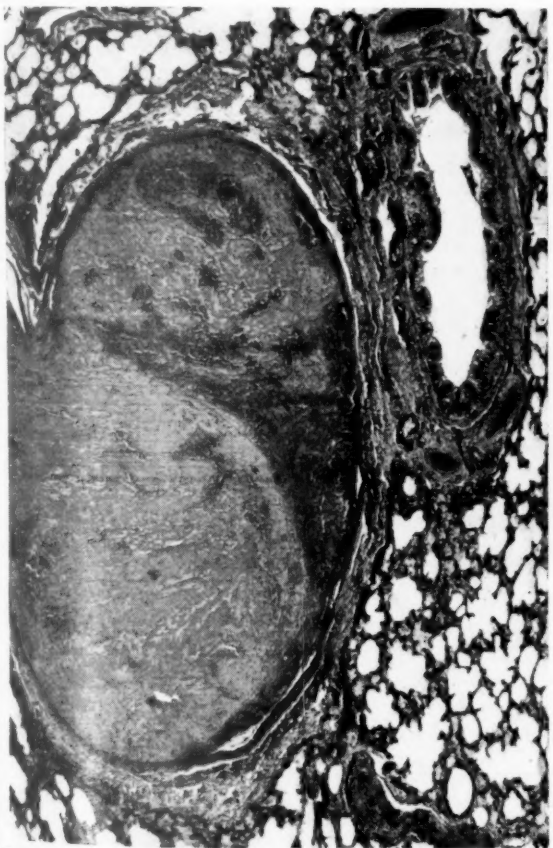

FIG. 5.—Thrombus in a large vein near a small bronchus. Masson trichrome ×40.

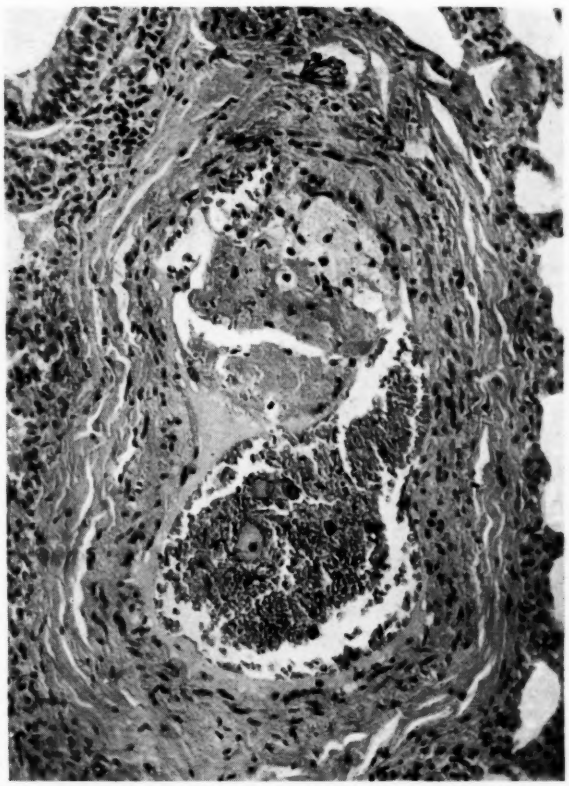

FIG. 7.—A thrombus partially occluding a small vessel and 'foamy' cell proliferation of the underlying intima. Masson trichrome ×150.

1937) and in adults has long been recognized in pulmonary thrombosis as the 'Michaelis symptom' (Möller, 1922). The importance of this symptom is probably increasing. Kallner (1948) considers that thrombosis of vessels in the lung in pneumonia is commonly why the temperature does not fall during antibiotic therapy. He noted a clinical response in these cases to anticoagulant therapy.

The absence of infarction in the present cases is not surprising. The experimental work of Chapman, Gugle and Wheeler (1949) suggests that embolism does not produce infarction of the lung unless some other pulmonary or circulatory factors are present. The small amount of alveolar haemorrhage seen in many cases may well represent minute infarction but such small haemorrhages are almost universal in deaths in infants. Hepler (1934), discussing thrombosis of renal veins, attempts to classify the thromboses on the site of the original thrombosis within the kidney but this seems to be of academic interest only, and I was unable to make any conclusive observations in the lungs. Vessels of all sizes seem to be affected in different cases but never all in the same case (Figs. 4, 5 and 6).

Abeshouse (1945) reviewed 228 cases of renal venous thrombosis from the literature and of these 98 occurred in the first year of life. Morison (1945) in one of his cases of renal thrombosis found thrombi in small pulmonary arteries—which he considers to be due to emboli of the kidney. It would seem from our cases that the same factors as those producing renal and cerebral thrombosis also cause pulmonary thrombi. Sandblom (1948) discussing renal thrombosis suggested that two types of thrombosis occurred in childhood, a rare, primary type occurring during the first week of life and a secondary, commoner type associated with dehydration. It would be simple to suggest that in the cases where we found a history of diarrhoea or vomiting that thrombosis was due to secondary haemoconcentration, and in the other cases that the condition was primary. But such an explanation would be a little naive. Many children with very severe dehydration do not have thromboses, and factors such as endothelial cells, acute circulatory failure, changes in factors related to blood coagulability such as antithrombin, may each play a precipitant role in different cases.

Zuelzer, Kurnetz and Fallon (1951) in describing thrombosis in infancy consider the chief to be haemoconcentration, slowing of the blood stream and damage to the endothelium. The only vascular endothelial change seen in the present cases were one (Fig. 7) showing intimal changes probably secondary to thrombosis and the other an endarteritis of long standing in a single vessel. Without more evidence it seems pointless to speculate further as to the aetiology of the thrombosis; the most fruitful cases for study seem to be those in Group II where vascular thrombosis occurs while the patients are in hospital under treatment.

It is not justifiable to say that pulmonary thrombosis was the primary cause of death in these children. The presence of ante-mortem thrombi and of alveolar oedema does suggest that the lesion was the terminal incident. Those children having symptoms before death suggest that the pulmonary thrombosis was a major factor in death. In the children who were observed in hospital before the onset of pulmonary thrombosis an increased loss of fluid from the body had occurred. This suggests that haemoconcentration and increased viscosity of the blood may have been a factor in the formation of the thrombosis, but we have no data on the blood coagulation in these infants.

From a clinical viewpoint, however, if an ill child develops unexpected pyrexia and dyspnoea associated with loose stools or vomiting, venous thrombosis should be actively considered, and anticoagulant therapy is indicated, particularly if there is no response to antibiotics.

Summary

Fifteen cases of pulmonary vascular thrombosis with alveolar oedema in children are described.

The cases occurred in four clinical groups: (*a*) severely debilitated neonates; (*b*) children severely ill for a long period; (*c*) children admitted to hospital with severe dyspnoea; (*d*) children found dead and referred to the Coroner.

In children observed before death, symptoms of pulmonary thrombosis, which consist of pyrexia and dyspnoea showing no response to antibiotic therapy, are frequently preceded by a history of loose stools or vomiting.

Care in maintaining fluid intake and tissue hydration in debilitated infants may prevent the onset of thrombosis, but we have no knowledge of the cause of the thrombosis in many cases.

Where thrombosis has occurred anticoagulation therapy would seem reasonable in addition to the usual antibiotics.

The cases in this study were under the care of Dr. T. Colver, Dr. R. R. Gordon, Dr. M. Middleton, Professor R. S. Illingworth, and Mr. R. B. Zachary, and their case notes have been freely used. The sudden deaths were referred by Mr. C. G. Lockwood. I am grateful to Miss C. Crawley for her help in obtaining case histories in the cases of sudden death.

Photographs by Mr. A. Tunstill.

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BLOOD SUGAR STUDIES ON PREMATURE BABIES*

BY

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The blood sugar has been extensively studied in normal infants. There is a great variation in the published results (Ketteringham and Austin, 1938; Hartman and Jaudon, 1937). Norval, Kennedy and Berkson (1949) found mean fasting values of 56 mg. on the first day, 54·9 mg. on the second day, 57 mg. on the third day and a gradual rise to 69 mg. on the fifth day. All workers have found that the results vary over a very wide range. Clement Smith (1951) states that the range is so wide that a 'normal' figure is of very little value.

Similar investigations on premature infants have been less numerous, especially in the first two days of life. Van Creveld (1929) found levels of 51 mg., 31 mg. and 60 mg. on the second day. Miller and Ross (1940) found a mean value of 32 mg. on the first day, with a range of 19 mg. to 44 mg. Norval (1950) found levels of 45 mg. and 53 mg. on the first and second days, with a continuous rise until the fourteenth day. She also performed serial readings on four infants during the first day of life and found a rapid fall over the first four hours, a slower fall for another eight to 12 hours and a slight rise during the following 12 hours. Over the next day the levels rose in two of the infants and fell in the other two.

Material

One hundred and fifty-four determinations were made on 21 infants weighing 5 lb. 8 oz. (2,500 g.) or under at birth. Only four of the infants received feeds during the period of observation. These infants received 5% glucose in quantities approximating to 0·4 g. per kg. An effort was made to collect a specimen from each child every six hours for the first 48 hours. A number of infants died before the 48-hour period was completed. The first specimen was taken from the placental end of the umbilical cord. Subsequent specimens were obtained by heel-prick. The Nelson-Somogyi method was used. The object of the investigation was to determine the blood sugar levels of premature infants in the first two days of life, with particular reference to the effect of birth weight, jaundice, neonatal distress and survival. The liver glycogen level was determined after death in 10 infants to ascertain the effect of starvation. The method used was that of Eufinger (1932).

Results

The mean cord-blood sugar was 66 mg. per 100 ml. with a range of 40 mg. to 140 mg. The mean post-natal level was 45 mg., with a range of 16 mg. to 90 mg. The most striking characteristic noted was the extreme variability of the blood sugar level. Wide fluctuations occurred in the series as a whole and in the individual curves.

There was practically no difference between the mean levels on the first and second days, 44 mg. and 45 mg. respectively. The readings were divided into six-hour groups from birth onwards (Table 1).

TABLE 1

RELATIONSHIP BETWEEN BLOOD SUGAR AND AGE

Age (hours)	No. of Determinations	Mean	Standard Deviation	Highest Level	Lowest Level
0-6	20	47·4	28·3	72	26
12	23	45·1	20·6	107	18
18	23	43·2	18·4	62	15
24	14	42·8	15·0	60	16
30	15	44·2	25·3	90	18
36	10	40·8	11·9	60	25
42	14	45·7	17·5	78	18
48	14	50·0	17·4	80	19

There was no significant difference between the various age-groups, with one exception. The value of 50 mg. found in the final period is significantly higher than that found in the sixth period. It will be noted that the sixth period contains the smallest number of determinations.

No relationship was found between the blood sugar level and the birth weight (Table 2). The only groups which showed a significant difference were the 3 lb. to 3 lb. 15 oz. group and the 5 lb. to 5 lb. 8 oz. group. Again the latter was the smallest group

* Based on material used for an M.D. thesis.

TABLE 2

RELATION OF MEAN POST-NATAL BLOOD SUGAR TO BIRTH WEIGHT, EXCLUDING CORD-BLOOD DETERMINATION

Birth Weight (lb. oz.)	No. of Cases	No. of Determinations	Highest Level (mg.)	Lowest Level (mg.)	Mean (mg.)	Standard Deviations (mg.)
Under 3	6	33	107	18	47·1	14·1
3-3 15	5	30	85	36	56·3	11·3
4-4 15	6	40	96	18	45·2	13·3
5-5 8	4	30	66	15	34·2	12·7
Total	21	133	107	15	44·4	15·9

in the series. Similarly the cord blood sugar showed no relationship to the birth weight (Table 3).

TABLE 3

RELATION BETWEEN CORD BLOOD SUGAR AND BIRTH WEIGHT

Weight (lb. oz.)	No. of Cases	Mean (mg.)	Standard Deviation (mg.)	Highest Level (mg.)	Lowest Level (mg.)
Under 3	6	73	27·5	100	56
3-3 15	5	78	28·4	116	40
4-4 15	6	62	30·2	84	44
5-5 8	4	73	25·3	140	24

The infants were divided into two groups, the moderately jaundiced and the severely jaundiced. The validity of this distinction will be referred to later. It was found that the severely jaundiced babies had a significantly higher blood sugar level than the moderately jaundiced (Table 4).

TABLE 4

RELATION OF BLOOD SUGAR TO SEVERITY OF JAUNDICE

	No. of Cases	No. of Determinations	Mean (mg.)	Standard Deviation (mg.)
Severe jaundice	8	55	54·1	11·9
Moderate jaundice	12	72	41·2	10·4

Eight infants in the present series were considered to be distressed (Table 5). Distress was assessed clinically by the presence of cyanosis, flaccidity, twitching or gasping respirations. One infant was excluded from Table 5 and the subsequent two tables. The mother of this infant was a diabetic and the case was excluded because of the known morbidity of such infants in the neonatal period. The blood sugar level of the distressed and the non-distressed groups showed no striking difference.

TABLE 5

RELATION OF MEAN POST-NATAL BLOOD SUGAR LEVEL TO NEONATAL DISTRESS

	No. of Cases	No. of Determinations	Mean (mg.)	Standard Deviation (mg.)
Distressed	8	35	50	11·8
Non-distressed	12	92	44	12·2

Seven infants in the series died (Table 6). Post-mortem examination was carried out in five cases.

TABLE 6

RELATION OF MEAN POST-NATAL BLOOD SUGAR LEVEL TO DEATH OR SURVIVAL

	No. of Cases	No. of Determinations	Mean (mg.)	Standard Deviation (mg.)
Died	7	41	43·1	9·5
Lived	13	86	48·2	16·5

The cause of death in three was intranatal asphyxia and in the other two it was intracranial haemorrhage. The remaining two deaths were ascribed to intracranial injury on clinical grounds. There was no significant difference between the blood sugars of those who survived and those who died.

The relation of the blood sugar to distress was further investigated by noting the time at which the clinical manifestations of distress were most marked or death appeared imminent, and comparing the blood sugar level about this time with the previous mean (Table 7).

TABLE 7

BLOOD SUGAR LEVEL NEAREST TIME OF GREATEST DISTRESS OR DEATH

No.	Result	Previous Mean (mg.)	Value at Time of Most Distress (mg.)	Difference
1	Lived	60	36	−24
2	Lived	43	86	+43
3	Lived	70	107	+37
4	Died	36	46	+10
5	Died	48	37	−11
6	Died	53	26	−27
7	Died	61	18	−43
8	Died	29	55	+26

The results showed no constant trend. Thirty-one readings of 30 mg.% or less were found in the series. The clinical condition at the time of these low levels has been considered. Only on four occasions was there an association between a blood sugar level of less than 30 mg. and clinical evidence of distress.

The liver glycogen content after death was estimated (Table 8). None of these infants had been fed. The figures are influenced to a considerable extent by the delay between death and the removal of the liver. This was occasioned by the necessity for obtaining permission from the parents. Allowing

TABLE 8

LIVER GLYCOGEN CONTENT AFTER DEATH

No.	Maturity	Weight (lb. oz.)	Time Survived	Interval* (hours)	Result (mg.%)
1	28 weeks	2 3	3 days	Nil	340
2	28 weeks	2 0	4 days	Nil	45
3	28 weeks	3 0	4 hours	52 hours	400
4	36 weeks	4 14	41 hours	Nil	33
5	40 weeks	6 0	S.B.	16 hours	1,670
6	40 weeks	6 8	1 hour	14 hours	2,500
7	30 weeks	2 14	38 hours	70 hours	9
8	36 weeks	5 4	22 hours	30 hours	40
9	34 weeks	3 10	16 hours	16 hours	200
10	40 weeks	6 10	25 mins.	8 hours	1,748

* The figure in this column denotes the interval that elapsed between the death of the infant and the determination of the liver glycogen.

for this time lag the cases examined showed a depletion of liver glycogen which was well marked within 12 hours of birth.

Discussion

The mean value for the blood sugar in the first day of life is almost identical with that found by Norval (1950) using a similar technique. Norval's figure for the second day is 53 mg. as against 45 mg. in the present series. The difference may be due to the fact that the infants in this series received no feeds, or feeds of negligible sugar content on the second day. This would suggest that premature infants behave like full-term infants in that their blood sugar levels remain low until feeding is begun. Kugelmass, Berggren and Cummings (1933), van Creveld (1929) and Norval (1950) drew attention to the absence of symptoms with hypoglycaemia in newborn premature infants.

The absence of a connexion between the birth weight and the blood sugar level is common to the findings of all investigators. This is interesting in view of the fact that liver glycogen increases with maturity. Windle (1940) states that this is true for all mammals. Clogne, Welti and Pichon (1924) and Eufinger (1932) have shown that it is true for man. The premature infant is less well equipped to withstand carbohydrate deprivation than the full-term infant. This draws attention again to the significance of starvation in the production of low blood sugar levels. The absence of correlation with the birth weight indicates that even moderately large glycogen stores are depleted by starvation. Lund, quoted by Huggett (1941), states that embryonic glycogen appears to have a different constitution from adult glycogen. In this difference may lie some reason for the absence of relationship between the birth weight and the blood sugar. The increase in liver glycogen towards term is accompanied by a decrease in placental glycogen. This alteration in the placental glycogen is not reflected in the cord blood sugar, indicating that at birth the foetus has already assumed control over the blood sugar.

Van Creveld (1929) held that the blood sugar was low in premature infants because of functional immaturity of the regulating mechanism, in which he gave pride of place to the liver. He did so because of the low glycogen content of the liver in premature animals and because of the evidence that physiological jaundice indicated hepatic dysfunction. This view of physiological jaundice is now accepted (Smith, 1951). Further evidence of the inadequate excretory function of the liver in the newborn is found in the work of Yudkin, Gellis and Lappen (1949) and Mollison and Cutbush (1949) who found a marked delay in the excretion of bromsulphalein in the early days of life in normal newborn infants. No comparable studies have been made on premature babies. Halbrecht and Brzoza (1950) found no difference between the albumin-globulin ratio, serum Van den Bergh reaction, thymol and cephalin flocculation tests in premature and full-term infants. This conflicts with the common experience of the greater frequency of icterus in premature infants.

In the present series the severely jaundiced infants had higher blood sugar level than the moderately jaundiced. The distinction between the two groups was clinical and it must be accepted that the clinical assessment of jaundice is often made difficult by changes in the vascularity of the skin and by the presence of anaemia. Furthermore, many premature infants show some degree of jaundice. With these reservations the present work indicates that impairment of the excretory function of the liver is not necessarily accompanied by failure of carbohydrate control and that the liver glycogen stores are more important than theoretical failure of the release mechanism.

In the absence of large liver glycogen stores the maintenance of the blood sugar level is dependent on gluconeogenesis. This is controlled by the corticoids of the suprarenal. There is evidence that suprarenal function is deficient in the first few days, although it subsequently reaches adult standards. Talbot, Zygmuntowicz, Wood and Christo (1950) found that the corticoid excretion per unit body surface was constant throughout life, apart from the first few days when it was low. Venning (1950) found no rise in the corticoid excretion after A.C.T.H. injection on the second day. The circulating eosinophils were found to be low in the first two days by Lippman (1924) and Klein and Hanson (1950). The latter also found an inadequate response in the eosinophil count following injection of A.C.T.H. White and Sutton (1950) found that the eosinophils did not fall after injection

of adrenalin in premature infants under 2,270 g. weight. Desmond, Hild and Gast (1950) found no striking response in the blood sugar following adrenalin. Selye (1946) described the effect of stress on the blood sugar; a rise in the stage of alarm, fall during resistance and a further rise following exhaustion. The absence of a consistent glycaemic response to stress in the present series and in that of Liebe (1940) is confirmatory evidence of suprarenal hypofunction.

A further factor in the regulation of the blood sugar is insulin. Nakamura (1924) described an excess of islet cells in foetuses and newborn infants. Fisher and Scott (1934) found a gradual decrease in the insulin content of calf pancreas from the fifth antenatal month to the early post-natal period. Even then the insulin content was higher than adult levels. The effect of this is counteracted by the increased resistance of foetuses of all species to insulin. Hartman and Jaudon (1937) confirmed this to some extent in human newborn infants.

Summary

The blood sugar has been studied in premature babies in the first two days of life. Low levels have been found but these were not associated with abnormal symptoms. It is suggested that they are due to a low liver glycogen content, which is depleted by starvation. The endocrine control of the blood sugar in premature babies is discussed.

My thanks are due to Dr. F. P. Hudson, consultant paediatrician, for encouraging me to perform this investigation in the Premature Baby Unit at Walton Hospital; to Dr. R. McLaren Todd, senior lecturer in child health, who revised the manuscript for publication; to Mr. R. Crosbie, B.Sc., and Miss P. Kennedy, B.Sc., who carried out the glycogen estimations, and to Mr. K. Kenyon, B.Sc., for the statistical analysis.

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INTRACRANIAL BRUITS IN INFANTS AND CHILDREN

BY

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The first recorded description of intracranial bruits was by Fisher (1834) who heard a 'cephalic bellows sound' in six children suffering from hydrocephalus. He thought that the sound was arterial in origin and that it was produced by pressure of the distended brain on the arteries at the base. The first description in this country was by Smyth (1837 and 1839) who heard a cerebral murmur in four children suffering from hydrocephalus. German and French physicians took an active interest in this murmur and their observations were reviewed by Jurasz (1877) and Epstein (1878). These writings reflect differences of opinion as to the significance of intracranial bruits, some observers maintaining that they were physiological and others that they were due to pathological conditions such as hydrocephalus, anaemia or rickets. Jurasz thought that the murmur developed because of a temporary relative stenosis of the carotid artery in the carotid canal, the foramen of which did not enlarge sufficiently rapidly. Henoch (1889) held that the murmur was of no interest from a clinical point of view and that it could not be turned to account for diagnosis. Osler (1880) also thought that the murmur had no special pathological significance. Still (1921) heard a cephalic bruit in 30 out of 200 children but he was unable to connect the bruit with any particular morbid condition. Rickets and anaemia did not occur with any frequency in his cases. Hamburger (1931) reviewed the conditions which may give rise to head murmurs, including arteriovenous aneurysms, meningiomas, gliomas and atheromatous lesions in young patients. Ford (1944) considers that anaemia is the most common cause of benign intracranial bruits in infancy and childhood.

During the past 30 years little interest has been taken in intracranial bruits by the paediatrician and the general physician. The neurologist has regarded them of importance if other evidence of neurological disease was present. With the development of intracranial surgical technique and more recently of cerebral angiography this physical sign is now of the first importance and we thought it opportune to reinvestigate the frequency and significance of intracranial bruits in infancy and childhood.

Present Investigations

Three hundred and one patients under 16 years of age in two children's hospitals in Liverpool have been examined and an intracranial murmur was heard in 34 patients. The age distribution is given in Table 1, which also records Still's figures for comparison. The children examined were suffering or convalescing from such common conditions as bronchitis, pneumonia, gastro-enteritis, congenital and rheumatic heart disease, and a few were being investigated for neurological disorders such as petit mal and hydrocephalus. The diagnoses of the patients in whom intracranial bruits were heard are recorded in Table 2, but the remaining 267 children were suffering from similar illnesses.

TABLE 1

	This Series			Still (1921)		
Age	Cases	Bruits	%	Cases	Bruits	%
0–	65	9	13·8	47	7	14·9
1–	28	5	17·8	25	10	40
2–	23	3	13·0	16	2	12·5
3–	24	3	12·5	19	7	36·8
4–	19	5	26·3	23	0	—
5–	26	3	11·5	12	0	—
6–	15	1	6·6	10	1	10
7–	21	2	9·5	8	1	12·5
8–	6	1	16·6	11	0	—
9–	10	0	—	8	1	12·5
10–	13	1	7·7	7	0	—
11–	16	0	—	5	0	—
12–	12	0	—	1	0	—
13–	9	1	11·1	3	0	—
14–	8	0	—	2	0	—
15–16	6	0	—	3	1	33·3
Totals	301	34	11%	200	30	15%

It was interesting to observe that in most of the children the breath sounds were distinctly heard while listening for the intracranial bruit, but the heart sounds could not be detected. In two children with congenital cardiac lesions an intracranial bruit was heard, but in 15 children with a loud cardiac murmur resulting from congenital or rheumatic

TABLE 2

ILLNESSES OF CHILDREN WITH INTRACRANIAL BRUIT

Primary pulmonary tuberculosis	5
Bronchitis	4
Pneumonia	4
Feeding error	2
Burns	2
Glandular fever	2
Congenital heart disease	2
Empyema (convalescent)	1
Hydronephrosis	1
Upper respiratory tract infection	1
Coeliac disease	1
Meningococcal meningitis	1
Poliomyelitis	1
Abscess in groin	1
Tuberculous glands in neck	1
Fractured femur	1
Erythema multiforme	1
Chorea	1
Hodgkin's disease	1
Nephritis	1
	34

heart disease no intracranial bruit was heard. A number of children were suffering from conditions such as leukaemia in which marked anaemia was present but in none of these children was an intracranial bruit heard.

Discussion

Our observations are in agreement with those of Still (1921) that an intracranial bruit can be heard in 10 to 15% of children suffering from some of the common clinical conditions. This bruit, which is best heard in the temporal region, varies in intensity, and, while in some children it is easily heard, in others it can only be heard when they stop breathing. Most observers agree that the bruit is arterial in origin and in our cases the bruit disappeared when the carotid artery was compressed. In some of our cases the cervical lymphatic glands were enlarged but not sufficiently to impede the flow of blood through the carotid arteries. We have not had an opportunity so far of examining at necropsy the internal carotid arteries of any of our patients in whom an intracranial bruit was heard during life. It is our intention, when opportunity offers, to outline the carotid arteries of such patients with latex, and to examine them with particular reference to calibre and tortuosity. It is possible that the petrous portion of the carotid artery may be narrowed as it passes through the bony carotid canal, and that the difference in calibre of this part of the artery and the intracranial (cavernous) portion may be responsible for the production of the bruit.

The frequency with which intracranial bruits are heard diminishes with age. In Still's series a bruit was heard in four out of 93 children aged 4 years or over compared with 26 out of 107 children under this age. In our series the bruit was heard in 15·7% of children under 5 years of age, in 9·1% aged 5 to 9 years, and in 3·4% aged 10 to 15 years. In adults, an intracranial bruit is heard infrequently, and when present it is usually indicative of organic disease, but in children an intracranial bruit is a relatively common finding; it is more likely to be heard in the younger age groups, and it does not usually indicate organic intracranial disease.

Idiopathic epilepsy is not an uncommon disorder in children; it would not therefore be surprising to find that some children had both an intracranial bruit and epilepsy. One such child, aged 7 years, not included in the present series, has been observed and bilateral angiograms performed but these did not reveal any vascular abnormality.

It has been found that cranial bruits (both 'functional' and organic) can easily be recorded with a phonocardiograph. Fig. 1 is a record of the bruit of the above child and Fig. 2 for comparison is a record of a bruit arising in a cerebral angioma in a woman of 40 years. In each case an E.C.G. (lead 2) is recorded simultaneously. It is of interest that both bruits when recorded show first and second sounds which cannot be distinguished clinically.

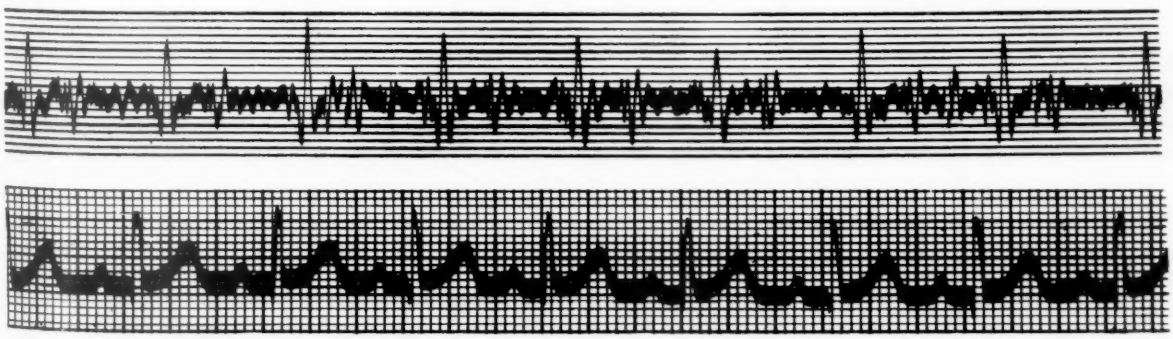

FIG. 1.—Phonocardiographic and electrocardiographic records from a girl aged 7 years in whom an intracranial bruit was heard but in whom bilateral cerebral angiograms showed no abnormality.

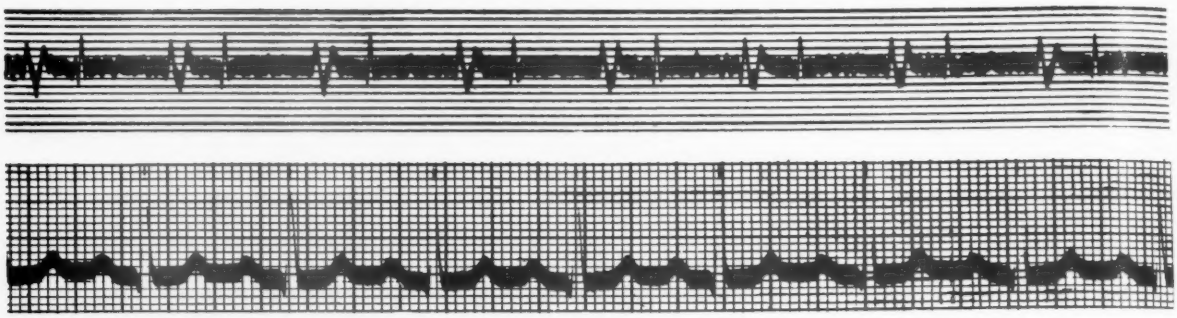

FIG. 2.—Phonocardiographic and electrocardiographic records from a woman aged 40. Intracranial bruit was heard and cerebral angiograms revealed an angioma of the left parietal region.

Conclusions

From our observations it would be reasonable to conclude that the presence of an intracranial bruit in a child does not, of itself, indicate that an organic lesion, such as a cerebral aneurysm or vascular malformation, is present, and is not sufficient justification for subjecting children to cerebral angiography or similar procedure.

We are indebted to Professor Sir Geoffrey Jefferson for his helpful criticism and to Mr. Caldwell for the phonocardiographs.

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RUPTURE OF THE FOETAL HEART DURING LABOUR

BY

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(RECEIVED FOR PUBLICATION FEBRUARY 9, 1953)

A case is reported in which haemopericardium, resulting from rupture of the foetal heart during labour, was the cause of death in a stillborn infant.

Case Report

Obstetrical History. The mother, aged 28 years, gave a history of two miscarriages about the eighth and tenth weeks of pregnancy in 1947 and 1951. During the present pregnancy she had been attending the ante-natal clinic and her general condition was considered satisfactory but, on June 12, 1952, about the thirty-ninth week of pregnancy, she was admitted to hospital on account of pitting oedema of the ankles, legs and abdominal wall. On admission, her blood pressure was 134/90 mm. Hg and the urine was free from protein.

History of Labour. The presentation was a vertex and clinically there was no cephalo-pelvic disproportion. Pelvimetry also showed the pelvis to be adequate. On June 12, 1952, a quinine induction (four doses of quinine hydrochloride, gr. 5, at four hourly intervals) was given, followed by 'pitocin' (six doses of 2 i.u. at half-hourly intervals) to induce labour. (The expected date of confinement was June 18, 1952.) On June 13, the membranes were ruptured surgically as labour had not begun. After this, labour proceeded normally; a bilateral sympathetic block was performed with good relief during the first stage. The first stage lasted 11 hours and 40 minutes. A local pudendal block was performed at the start of the second stage. The head advanced slowly and, because of delay in delivery of the head, an episiotomy was performed. Following delivery of the head, difficulty in delivering the shoulders was experienced: this was easily overcome by placing fingers in the axillae and exerting traction. No difficulty was encountered thereafter. The second stage lasted for one hour and 50 minutes.

A stillborn male infant weighing 8 lb. 6 oz. (3·8 kg.) was born. The foetal heart sounds had been regular during labour, the last recording being made 10 minutes before delivery. Although the baby was stillborn it was considered advisable, at the time, to attempt to establish respiration; this was done by intubation and oxygen insufflation. An intracardiac injection was not given.

Necropsy. The infant was well nourished and there were no external physical malformations. Oedema, jaundice and cyanosis were absent. A prominent caput was present over the vertex.

On opening the thorax the pericardial sac was seen to be distended with blood. The sac was opened: fresh blood escaped and a blood clot, approximately 15 mm. in diameter, lay along the left border of the left ventricle. Carefully turning the apex of the heart upwards, the diaphragmatic surface and base of the heart were examined. A small hole, through which a clot of blood protruded, was observed in the lower and posterior part of the right atrium just anterior to the point of insertion of the inferior vena cava. This tear, approximately 6 mm. long × 1-2 mm. broad, involved mainly the membranous portion of the atrial wall but extended into the muscular part, and extravasation of blood within the wall could be seen over an area adjacent to the site of rupture (Fig. 1). The other cardiac chambers, valve orifices and cusps, and the myocardium presented no abnormal features.

The lungs showed evidence of very slight aeration. In the abdomen, apart from moderate congestion of the liver, no abnormality was seen. The brain was normal.

Discussion

Haemopericardium, resulting from rupture of the foetal heart, is extremely rare. Two cases in stillborn infants, in addition to the present one, have been reported, one by Longridge (1907) and one by Hunt (1952). One case of haemopericardium in a stillborn infant, not associated with rupture of the heart, was reported by Silbernagel and Fidler (1943) and another case of haemopericardium, again in a stillborn infant, in which the precise site of bleeding was not determined, was described by Potter (1952).

The case reported by Longridge (1907) was one in which a shoulder presentation at full term was admitted to hospital with a prolapsed and pulseless cord. After craniotomy and powerful traction a child, weighing 9 lb. 5 oz. (4·22 kg.), was born. Necropsy revealed a haemopericardium with rupture of the heart at the junction of the inferior vena cava and right atrium. In the case described by Hunt (1952) the foetus, weighing 5 lb. 11 oz. (2·58 kg.), was delivered as an assisted breech; the foetal heart sounds had been heard earlier in labour. In this case, a perforation, measuring less than half a millimetre in diameter, was found situated in the anterior wall of the right atrium close to the root of the atrial

FIG. 1.—Necropsy specimen showing the diaphragmatic surface and base of the heart with the rupture and adjacent area of bruising in the right atrial wall.

appendix. The perforation was attributed to a focal hyaline degeneration of the myocardium, of unknown aetiology, at the point of rupture. The cases described by Silbernagel and Fidler (1943) and Potter (1952) were similar to each other in that in each case the mother gave birth to a stillborn infant following an accident. In the former case the mother had been involved in a car accident in which she was thrown from the car and struck her abdomen on the kerb of a pavement, and in the latter the mother had fallen down a flight of stairs two days before delivery.

The tear in the atrial wall in our case was not an artefact produced at the time of necropsy. Histological examination of the atrial wall near the site of rupture shows extravasation of blood between muscle fibres, an ante-mortem change (Fig. 2). Moreover, comparison by histological examination of the atrial wall at the site of rupture with the corresponding part in normal foetal hearts has shown no evidence of any difference in thickness of the wall to suggest a congenital anomaly or any degenerative change in the muscle fibres. Assuming the tear to have been traumatic in origin, consideration has been given to the mechanics whereby this might possibly have been produced. When it is recalled that in the foetus the liver at birth occupies the greater portion of the upper abdominal cavity and is relatively unprotected by the thoracic cage, it will be appreciated that considerable strain could be exerted on the inferior and superior venae cavae and the right atrial wall by pressure of the contracting uterus, either holding the liver fixed in position in the abdominal cavity or forcing it downwards towards the pelvis, and the tension, operating simultaneously and in the opposite direction, exerted on the mediastinum by traction on the head or shoulders. Attempts to reproduce this state of affairs have been made on the cadaver, and although rupture of the atrium has not been produced, considerable tension on the atrial wall can undoubtedly be exerted. During life an additional factor might well be a congested and tensely dilated right atrium with congested venae cavae such as might be the case during a labour more difficult than average. Under these conditions it is conceivable that the wall of the right atrium might tear about the site where the rupture occurred in the present case and in the case reported by Longridge (1907).

The possibility of an uterine contraction ring

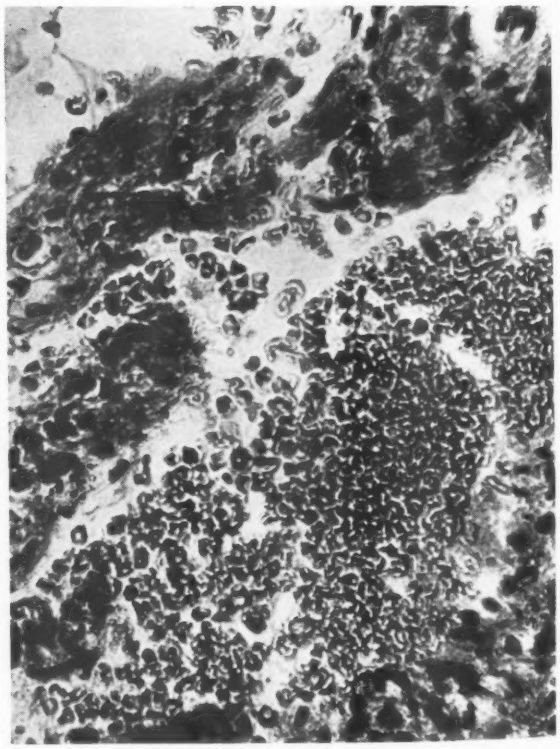

FIG. 2.—Photomicrograph showing extravasation of red blood cells between muscle fibres in the atrial wall. Haematoxylin and eosin × 300.

being responsible for the difficulty encountered in delivering the shoulders and exerting some unusually severe pressure on the viscera of the foetus is not considered likely, as, had it been so, one might have expected that further attempts to deliver the child without anaesthesia would have tended to aggravate the condition rather than prove beneficial.

In the case presented here, the delivery was in the hands of the nursing staff until one of us (A.G.) took over after difficulty with delivery of the shoulders had been encountered. There had been no undue torsion of the body. It is possible, although only conjectured, that the degree of traction exerted on the head, when difficulty in delivering the broad shoulders of the overweight infant was experienced, might have been considerably more powerful and protracted than would be exerted during the course of a normal labour. It is, however, difficult to envisage the precise aetiological factor responsible for this distinctly rare occurrence when the maternal pelvis, the foetus and course of labour were in no way widely divergent from normal.

This appears to be the third reported case of haemopericardium associated with rupture of the heart in a stillborn infant.

Summary

A case is described in which haemopericardium, resulting from rupture of the right atrium during labour, was found on necropsy to be the cause of death in a stillborn infant.

The rupture is considered probably to have been traumatic in origin, and factors concerned in the possible mechanism leading to this rare occurrence are briefly considered.

We wish to thank Mr. G. A. Craig for his helpful advice and criticism during the preparation of this paper. We are also indebted to Mr. P. Harrison for the photographs, and to Messrs. E. F. Hill and J. D. Musgrave for the preparation of the histological material.

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VASCULAR RING: A CAUSE OF CONGENITAL STRIDOR

BY

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Stridor beginning at, or soon after, birth is not an uncommon symptom. Such stridor is seldom severe, has a natural tendency to become progressively less marked, and in the majority of infants disappears entirely at the end of the first, or early in the second, year of life. Occasionally, some cause of laryngeal or tracheal obstruction is found and can, where possible and when necessary, be eliminated. Finally, a number of babies with congenital stridor succumb to asphyxia or recurrent pulmonary infections, usually before the age of 1 year.

It must be admitted that in the majority of cases where recovery is spontaneous, and of those who die, no satisfactory cause for the stridor is ever found. The possible causes fall into two main groups according to whether the larynx or the trachea is the site of obstruction.

Laryngeal stridor in the newborn may be due to an exaggeration of the infantile shape of the upper aperture of the larynx. The aryepiglottic folds are almost in contact, producing a purring, inspiratory stridor. There is no dyspnoea, no distress and no dysphagia, and the condition is recognized on laryngoscopy. Webs, cysts and tumours of the larynx are all excessively uncommon, and can be seen on laryngoscopic examination. Neuromuscular incoordination of the larynx has been suggested as a possible cause of congenital stridor: the condition, if it exists, should be recognizable on laryngoscopy.

Tracheal stridor in the newborn may be due to tracheal stenosis, but this condition is extremely rare, and the majority of cases are not sufficiently severe to cause symptoms. Bronchoscopy and contrast radiography will demonstrate the condition. The trachea may be pressed upon by an enlarged thymus, a congenital goitre, or anomalous great vessels in the superior mediastinum. These three conditions will be considered in more detail.

Thymic stridor is described by Cockayne (1947) as

> 'a respiratory stridor which may be present at birth or may develop during the early weeks of life. The stridor is more pronounced during inspiration, but both inspiration and expiration are stridulous. It may be continuous or paroxysmal. During a paroxysm of dyspnoea, the obstruction to respiration may be so great that cyanosis supervenes with lividity of the lips and tongue and retraction of the ribs. . . . In other cases there are syncopal attacks, in which the child becomes limp and cold and the respiration becomes almost imperceptible. The child usually recovers after a few minutes, but may remain unconscious for two or three hours. Some cases of hyperplasia (of the thymus) have been associated with a persistent hoarse cough, noisy nasal breathing, paroxysms of rapid respiration, or attacks of choking with cyanosis during feeds.'

Although occasional cases of thymic compression of the trachea are met, most authorities would agree with Nelson (1945) when he states:

> 'There may well be some doubt that the thymus causes compression of the trachea in any significant number of instances. There is no doubt that the thymus may cause widening of the upper mediastinal shadow, which may be eliminated by shrinkage of the thymic tissue by roentgen-ray therapy. It is of considerable moment, however, that the size of this shadow bears no relationship to the occurrence of symptoms of respiratory obstruction.'

Stone (1945), citing Hill (1933), states that

> 'congenital goitre is associated with inspiratory stridor which disappears in sleep but is aggravated by crying. Upon effort there is engorgement of the cervical veins and cyanosis. The cry is likely to be hoarse, and difficulty in swallowing is a common accompaniment. The infant tends to throw the head backward to facilitate respiration.'

Diagnosis is straightforward unless the thyroid gland lies in the superior mediastinum.

Compression of the trachea and oesophagus by a vascular ring causes stridor from birth, which is chiefly inspiratory and less marked during sleep. There is often a cough and particular susceptibility to pulmonary infections. These infants feed slowly, because of the respiratory difficulty, and tend to lie with the head retracted. Dysphagia usually becomes evident when semi-solid or solid foods are introduced into the diet.

The similarity between the clinical pictures of tracheal compression from these three causes is

obvious, and it is the purpose of this paper to suggest that a vascular ring may be responsible for congenital stridor in a greater proportion of cases than is generally recognized. Its recognition is important because affected infants with severe symptoms dating from birth almost invariably die if untreated, as shown in the review of Griswold and Young (1949), whereas diagnosis of the condition is straightforward, and the principles of treatment are clear.

Comprehensive classifications of the types of vascular ring have been worked out by Neuhauser (1946) and by Edwards (1948), but the multitudinous varieties fall into three main categories. Besides these, symptoms of oesophageal and tracheal compression may be caused by a single anomalous vessel, as in Bayford's (1789) original case of dysphagia lusoria.

In the first group there is a single aortic arch passing behind the oesophagus to descend on the opposite side (usually a right arch with a left descending aorta), the ring being completed by a ligamentum arteriosum or patent ductus arteriosus on the side of the descending aorta (Figs. 1*a* and 1*b*).

In the second group there is one complete aortic arch and one aortic rudiment, joining to form a descending aorta on either side (usually the left). The ring is completed by a ligamentum arteriosum or patent ductus arteriosus on the side of the aortic rudiment (Figs. 2*a* and 2*b*).

In the third group there is a complete double aortic arch encircling the trachea and oesophagus. The aorta may descend on either side (usually the left), and a ligamentum arteriosum or patent ductus arteriosus may or may not enter into the composition of the ring (Figs. 3*a* and 3*b*).

The embryology, symptomatology and diagnosis of vascular rings are discussed by Dolton and Jones (1952), who describe a child with double aortic arch and patent ductus arteriosus who underwent successful operation. The case presented here was distinguished by the severity of the symptoms which left little doubt that the child would not have survived without surgical intervention.

Case Report

Terence B., a boy born on April 17, 1952, was admitted to the Bradford Children's Hospital under Dr. R. L. Langley on May 12, aged 4 weeks. He was a second child, delivered normally at full term weighing 7¼ lb. There was no history of maternal illness during pregnancy. He had been fully breast fed for three weeks, then his feeds were supplemented with a cow's milk-and-water mixture on which he was gaining weight satisfactorily.

The history was of difficulty in breathing since birth. For three days before admission there had also been cough, fever and attacks of cyanosis and dyspnoea, for which systemic penicillin had been given.

He was a well nourished boy weighing 8¾ lb., with a capillary naevus nearly 25 mm. in diameter on the forehead. The rectal temperature was 98·4° F., the pulse rate 138 per minute and respirations 36 per minute. He was breathing with difficulty; inspiration was harsh and wheezy, and there was a sharp, dry cough. There was cyanosis of the fingers and ears, but no clubbing of the fingers. The percussion note of the chest was unimpaired; the breath sounds were harsh in all areas. The heart sounds were pure, and no abnormality was detected in any other system. Stridor was present at all times until operation and was always less marked during sleep. The child showed no tendency to hold the head retracted.

The pre-operative course was marked by alarming attacks, invariably following feeds, which he took rather slowly. At times these attacks occurred two or three times a day for several days in succession, but on one occasion he went for four weeks without an attack. The attacks, which lasted between five and 20 minutes, started with choking and congestion of the face. The initial cyanosis then gave way to pallor, the child became limp, and respirations ceased. The heart action became rapid and feeble, and during one attack the heart sounds became inaudible. Recovery began with infrequent, gasping respirations, followed by a gradual return of normal colour, normal respiratory rhythm, and consciousness.

The mechanism of these attacks appears to be as follows. The regular occurrence after feeds suggests that the precipitating factor was a distended oesophagus which compressed the trachea. Choking caused the oesophageal contents to spill over into the trachea, thus completely obstructing respiration, and causing unconsciousness. At this stage the baby was to all appearances dead, except that the heart continued to beat feebly. With approaching death the blood pressure would fall, thereby relieving the pressure of the constricting aortic ring, and allowing air to pass through the trachea once more. When this mechanism was appreciated, the baby was held upright for 10 minutes after the completion of each feed. On this regime he had only one attack in four weeks, and this was cut short by inverting the child and thereby draining the oesophagus and trachea.

These attacks were frequently followed by pulmonary infection, and the child had eight attacks of bronchopneumonia in five months. These responded to penicillin at first, and to aureomycin later, but there seems little doubt that the responsible organisms would have become resistant to all available antibiotics if the condition had been allowed to persist.

Laryngoscopy by Mr. J. S. Davidson in June, 1952, showed no abnormality of the larynx or vocal cords. In August an attempt was made to introduce mixed feeding, but it was evident that the child had great difficulty in swallowing thickened feeds and the trial had to be abandoned.

X-ray photographs with barium in the oesophagus (Figs. 4, 5 and 6) were taken by Dr. P. P. Franklin and showed clear evidence of compression by a vascular

1a

FIGS. 1*a* and 1*b*.—Plasticine model of the vascular ring formed by the right aortic arch, right retro-oesophageal aorta and ligamentum arteriosum. Fig. 1*a*—Left anterior oblique view. Fig. 1*b*—Right posterior oblique view.

1b

2a

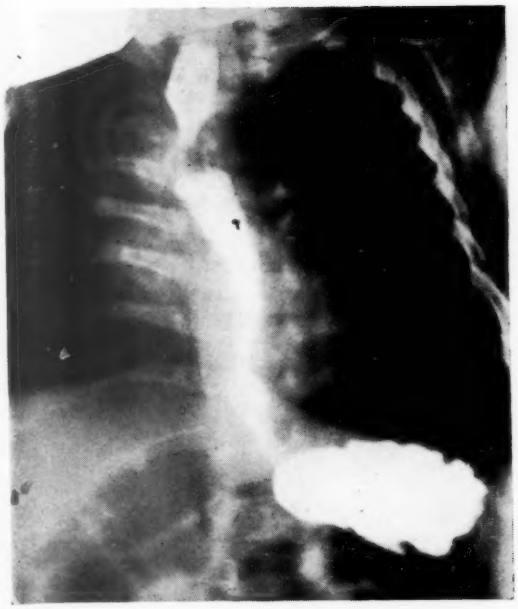
FIGS. 2*a* and 2*b*.—Plasticine model of the vascular ring formed by the right aortic arch, left aortic rudiment and patent ductus arteriosus. Fig. 2*a*—Left anterior oblique view. Fig. 2*b*—Right posterior oblique view.

2b

3a

FIGS. 3*a* and 3*b*.—Plasticine model of the vascular ring formed by the double aortic arch. Fig. 3*a*—Left anterior oblique view. Fig. 3*b*—Right posterior oblique view (pulmonary artery omitted for clarity).

3b

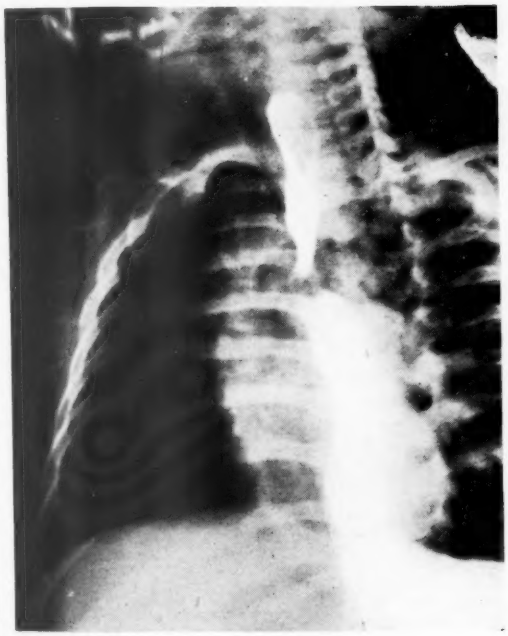


1b

4b

FIG. 4*a*.—Barium swallow: anterior view. Note bilateral constriction by the double aortic arch, and displacement of the oesophagus to the left below the constriction.

FIG. 4*b*.—Plasticine model: anterior view.



2b

FIG. 6*a*.—Barium swallow: left lateral view. Note the posterior indentation caused by the left retro-oesophageal aortic arch.

FIG. 6*b*. — Plasticine model: left lateral view.

6b

6a

3b

FIG. 5*a*.—Barium swallow: left oblique view. Note long, shallow, posterior indentation caused by the left retro-oesophageal aortic arch, and smaller anterior indentation.

FIG. 5*b*.—Plasticine model: left oblique view.

ring, with displacement of the lower oesophagus by a right-sided descending aorta.

Operation was undertaken by Mr. J. S. Davidson at the Bradford Royal Infirmary on October 8, 1952. The great vessels were approached from the left side and a left aortic arch identified. There was no evidence of a patent ductus arteriosus. The left arch was divided behind the origin of the left subclavian artery, and the cut ends sprang apart as if under considerable tension. Stridor and dyspnoea, which had hitherto made the anaesthetist's task extremely hazardous, were dramatically relieved, and the lung was seen to inflate and deflate much more readily.

The post-operative course was prolonged. Mixed feeding was introduced before the patient's discharge on the fourteenth post-operative day, and he swallowed semi-solids without difficulty. He was also able to take his feeds without any delay. He still had a slight cough on discharge, but it was an occasional, effective cough in sharp contrast to the ineffective cough before operation.

He was readmitted a few days later with mild bronchitis, but before he had fully recovered from this he developed very severe pneumonia, to which he almost succumbed. Convalescence from this illness was protracted, although he ate well, cut several teeth and gained weight satisfactorily.

When finally discharged three months after the operation, he was completely free from clinical and radiological signs of pulmonary disease.

Discussion

Although the great majority of vascular rings cause compression of both trachea and oesophagus, symptoms of oesophageal obstruction are usually inconspicuous while the infant is taking an entirely fluid diet. Such cases therefore present primarily with symptoms of tracheal compression, namely, stridor from birth, cough and an increased susceptibility to pulmonary infections. When these symptoms are encountered, the possibility of a vascular ring being responsible should be kept in mind, particularly if no abnormality is detected on laryngoscopy. Postero-anterior and lateral radiographs of the chest will usually show narrowing or displacement of the trachea at the level of the aortic arch, and contrast films with barium in the oesophagus will demonstrate clearly any constriction and give valuable information regarding the anatomical composition of any vascular ring. Angiocardiography may be necessary, but the introduction of iodized oil into the trachea should be avoided if possible. The recognition of this anomaly will not only allow of operative intervention, where this is indicated by the severity of the symptoms, but will also ensure that the infant is not subjected to the hazard of tracheotomy, which would increase the liability to pulmonary infection without in any way relieving the obstruction.

Summary

The causes of congenital stridor are considered, and the suggestion is made that tracheal compression by vascular rings arising from congenital anomalies of the great vessels may not be as uncommon as hitherto supposed.

A case is described in which severe symptoms of tracheal and oesophageal compression due to a bilateral aortic arch were dramatically relieved by operation.

This case is published by permission of Dr. R. L. Langley. To him, to Dr. E. Rosenblum and Mr. J. S. Davidson, I wish to express my gratitude for helpful advice and criticism. The photographs are by Mr. P. Harrison, M.S.R., of the Photographic Department, Bradford Royal Infirmary.

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CONGENITAL STIPPLED EPIPHYSES

BY

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From the Children's Hospital, Sheffield

(RECEIVED FOR PUBLICATION FEBRUARY 9, 1953)

Caffey (1950) suggested the term 'congenital stippled epiphyses' for a syndrome consisting of achondroplasia, radiological evidence of discrete centres of calcification in cartilaginous epiphyses, together with cataracts and mental deficiency. The condition was first described by Conradi (1914) under the title 'Chondrodystrophia Foetalis Hypoplastica', and was reviewed by Ford, Schneider and Brandon (1951). Below is a case record, presenting some unusual features, with necropsy findings.

Case Report

A girl, birth weight 6 lb. 8 oz., was born at home, after a normal pregnancy and delivery. The infant was admitted to the Jessop Hospital for Women at the age of 24 hours on account of cyanotic attacks. She was then found to have achondroplasia (Fig. 1), bilateral talipes equinovarus, a dry, wrinkled skin (Fig. 2) and bilateral cataracts. There was a grade 3 systolic murmur heard all over the precordium. She had no further cyanotic attacks, and was discharged, to be followed up in the Baby Clinic.

FIG. 1.—Photograph showing achondroplasia and slightly cretinoid appearance.

When she was 1 month old it was found that there was limitation of movement of the elbows, wrists and knees. There was a 70° flexion deformity of the knees, and similar limitation of extension in the elbows and wrists. It was thought that this might be due to a spastic quadriplegia, though the tendon jerks were not exaggerated. Radiological studies were made, however, in order to determine whether there was any bony lesion to account for the limited movements of the joints. The radiographs showed stippling of the epiphyses of numerous bones, but no obvious reason for the restricted extension (Figs. 3 and 4). The diagnosis of congenital stippled epiphyses was then made.

FIG. 2.—Dry wrinkled skin, with flexion deformity of the elbow.

There was a facial resemblance to cretinism, and the total serum lipoids were found to be 945 mg.%. Other serum chemistry gave serum calcium level, 11·2 mg.%, serum phosphorus level, 4·2 mg.%, serum alkaline phosphatase level, 16·0 units. She was given a six weeks' course of thyroid extract, without effect.

Other findings at the age of 1 month were defective head control when tested in the prone position, in ventral suspension and when pulled to the sitting position, and subluxation at the transverse tarsal joints.

During the next eight months she was followed up in the Baby Clinic, but she made very little physical or developmental progress. She was extremely difficult to feed, not appearing to be hungry, and at the age of 8 months her weight was only 7 lb. 3 oz. She did not appear to have increased in size at all. There had been hardly any progress in head control, for there was almost complete head lag, and she could only momentarily lift the chin off the couch in the prone position. She took no notice of sound. As she was blind, she could not be tested for eye-following. Vocalizations were very defective and slight. It was clear that she was

very severely mentally defective. The cardiac murmur had persisted. She died at the age of 9 months of an acute respiratory infection.

FIG. 3.—Stippling of epiphyses in shoulder, wrist and elbow. The areas of rarefaction in the upper end of the humerus may be enchondroses.

Necropsy. The immediate cause of death appeared to be an acute respiratory infection. Positive findings in other systems were as follows:

The heart was bifid at its apex but there was no atrial or ventricular septal defect. The foramen ovale was closed and the ductus arteriosus obliterated. There were pale gelatinous vegetations along the free edge of the mitral valve. No other valve showed gross changes. Histologically these vegetations consisted of masses of loose connective tissue of a myxomatous nature. No inflammatory changes were apparent (Fig. 5).

The liver was situated with the inferior edge almost vertical in the abdomen but showed no gross changes in structure. The kidneys were of normal weight. There was bilateral hydronephrosis with the hydro-ureter extending only to the brim of the skeletal pelvis. The eyes showed bilateral cataracts.

In the skeleton the skull was asymmetrical. The width of the ends of the long bones was grossly increased, owing to cartilaginous masses. The joints after removal of muscles could not be fully extended or flexed owing to the presence of these masses. On gross section there was great irregularity in colour and consistency of the epiphysis and some irregularity in the ossification line. The ribs and costal cartilage appeared to be relatively unaffected, as did the small bones of the hands and feet. In the spine the ossification centres were situated anteriorly and posteriorly, with a narrow waist between. The appearance of the spine was identical with the one illustrated by Harris in 1933 (Fig. 6). The histological appearance of the cartilage was similar to that illustrated by Harris, the most striking features being the variation in cellular concentration, the great increase in vascularity of the cartilage, and areas of apparent degeneration and primary calcification (Fig. 7). The vessels appeared to penetrate into the cartilaginous mass from the immediate joint surface. The ossification line in the rib, in the ends of the long bones and in the toes showed no specific abnormality. The cartilages of the toes and ribs appeared normal. No abnormality of structure was seen in the thyroid, ovary, retina, pancreas, adrenal, parathyroid, pituitary, brain and spinal cord. The lenses of the eyes were not examined histologically.

FIG. 4.—Stippling of the epiphysis in the knee joint.

FIG. 5.—Section of the mitral valve showing vegetation on the contact surface. Masson trichrome × 14.

Discussion

The anatomical features of this case are similar to those seen by others, but this child also had a congenital cardiac deformity and hydronephrosis with hydro-ureter.

Reilly and Smyth (1938) suggested that there was a connexion between congenital stippled epiphyses and cretinism. In this case the clinical impression of hypothyroidism, though supported by the finding of high total serum lipoids (947 mg.%), was not supported by response to treatment or by histological changes in the thyroid gland.

Much of the stippling in the epiphysis is due to calcification of apparently ischaemic areas of cartilage and not to the normal processes such as those in cretinism, but to abnormal growth of cartilage.

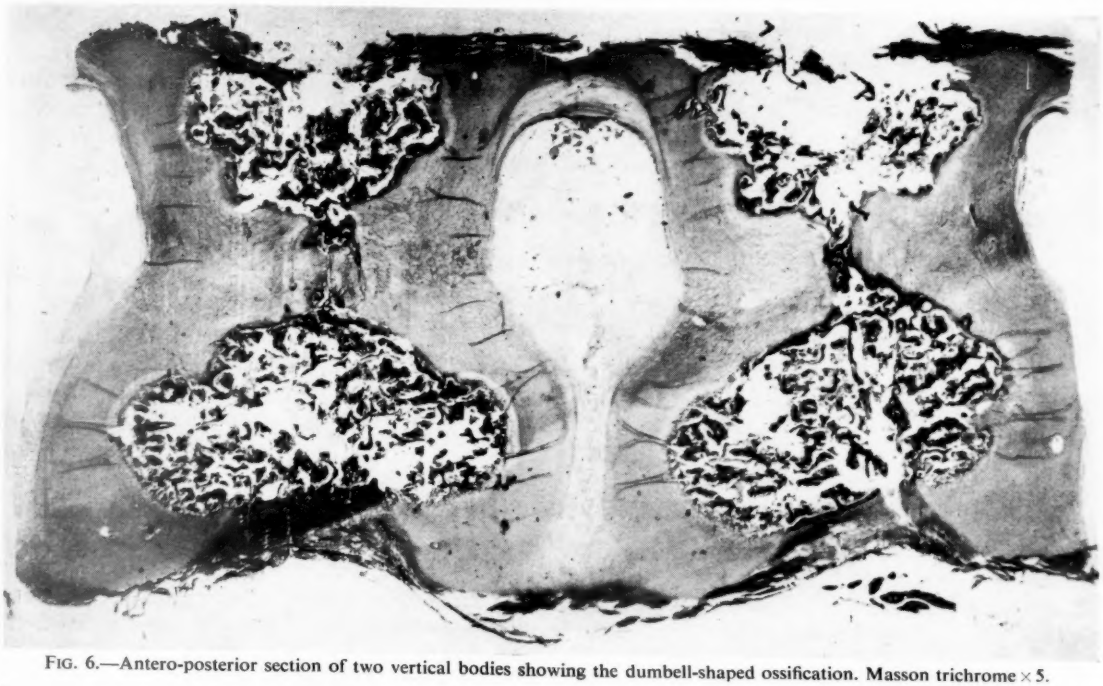

FIG. 6.—Antero-posterior section of two vertical bodies showing the dumbell-shaped ossification. Masson trichrome × 5.

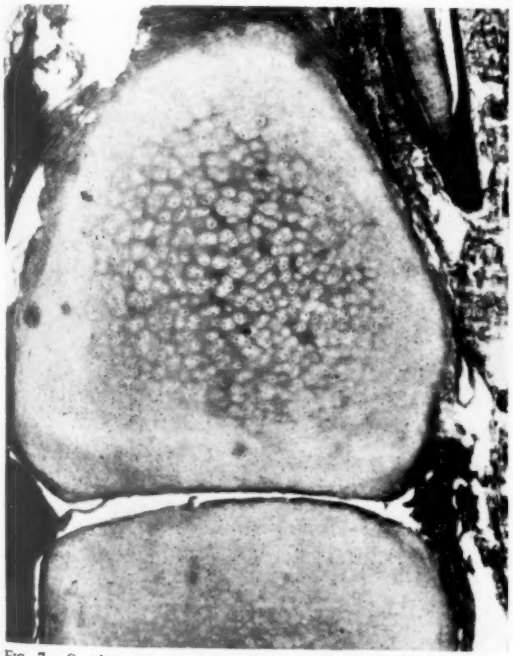

FIG. 7.—Section of cartilaginous mass at the head of the humerus showing gross abnormality of structure. Masson trichrome × 7.

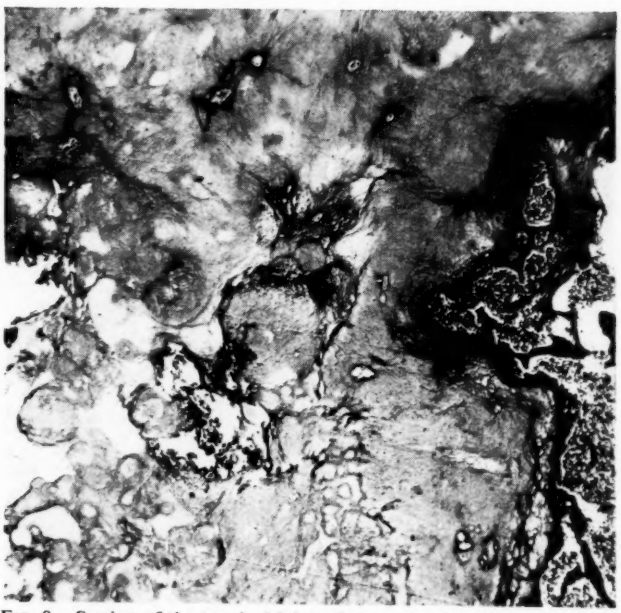

FIG. 8.—Section of the terminal joint of a toe showing normal cartilage and joint. Masson trichrome × 36.

The changes in staining properties of zones of cartilage, which Harris (1933) describes as 'mucoid', seem to us to be not a primary disturbance but merely a stage in degeneration of cartilage preceding calcification, such as is seen in many deformities or tumours of cartilage (Willis, 1948).

The disease affects apparently only the bones in which secondary centres of ossification in the epiphysis would be likely to develop *in utero*. The

FIG. 9.—Section of the upper end of the tibia showing a tongue of cartilage within the shaft of the bone. Masson trichrome × 6.

ends of the bones of the toes have completely normal cartilage (Fig. 8).

The abnormality in growth of the cartilage in this case appear to be similar in type to the chondrodysplasias, differing from them chiefly in the distribution of the abnormality in cartilaginous growth rather than in underlying structure. There is great variation within the chondrodysplasias themselves (Cole, 1926), but Fairbank (1927), on account of the distribution of atypical cartilage as seen radiologically, considers that cases of stippled epiphysis should not be included in the chondrodysplasias. In the present case there were some irregular masses of cartilage ('enchondrosis') penetrating into the shaft of the long bones (Fig. 9). Another abnormality of cartilage growth with a very similar distribution to the present case, multiple enchondroses, is believed by Speiser (1925) to be due to a fault in development occurring between the fourth and eighth month of foetal life. The abnormal vascularity of the cartilage in the present case is interesting in view of Bentzon's theory (1924) that unusual vascularity is the primary disorder in Ollier's disease or chondrodysplasia (Hunter and Wiles, 1935).

This child showed deformities of the mesenchymal tissue in the renal tract, the heart, and in the lens of the eye as well as in cartilage. This suggests to us, not that this child showed a particular syndrome or disease of connective tissue, but that the condition was due to some intra-uterine disturbance.

Our thanks are due to Dr. T. Lodge for the radiographs, to Miss Finch for the biochemistry, and to Mr. A. N. Tunstill, for the photographs.

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INCREASED HAEMATURIA IN NEPHRITIS DURING CORTISONE AND A.C.T.H. ADMINISTRATION

BY

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In the past few years cortisone and A.C.T.H. have been used in the treatment of nephritis. In the nephrotic state these drugs frequently produce a diuresis (Farnsworth, 1950a; Luetscher, Deming and Johnson, 1951). In haemorrhagic nephritis, however, the results have been variable (Thorn, Merrill, Smith, Roche and Frawley, 1950; Heller, Jacobson and Hammarsten, 1951).

The present paper reports an increase in the urinary red cell excretion which was observed in two cases of haemorrhagic nephritis which were treated with cortisone and A.C.T.H., and in one case, of doubtful diagnosis but thought to be haemorrhagic nephritis, treated with A.C.T.H.

Method

The method of measuring the haematuria was a modification of that described by Addis (1925). No special preparation of the patient, such as restriction of fluids, was carried out. Counts were made on the first morning specimens of urine. The patient was instructed to empty the bladder completely before going to sleep. The first morning specimen was collected, the volume and time over which the urine was secreted were noted, and, after thorough mixing, 30 ml. of urine was added to 0·25 g. of the preservative mixture recommended by the Metropolitan Life Insurance Company (Gradwohl, 1943). The red cells in 1 c.mm. of concentrated or unconcentrated urine were counted in a Fuchs-Rosenthal chamber. When the urine contained less than 100 red cells per c.mm. it was concentrated by centrifugation. The number of red cells excreted per hour was calculated.

Case Reports

Case 1.—A girl aged 13 was admitted to hospital in April, 1950, with gross haematuria and some oedema. She had been admitted to another hospital 18 months previously with the same symptoms, which had persisted ever since. On admission she was oedematous, and the urine contained numerous red cells, some granular casts and protein. The blood pressure was 140/90 mm. Hg and the fundi were normal.

In spite of a period of rest in bed, the patient deteriorated and developed gross oedema, ascites and bilateral pleural effusions. In addition, the blood pressure rose to over 200/130 mm. Hg and retinal haemorrhages and exudates with papilloedema developed. A.C.T.H., prepared by Dr. Max Reiss and kindly supplied by him, was then given for four days with little effect save that the patient stated that she could see better. A few days later, however, the publication containing Farnsworth's (1950b) first results in nephrotic patients arrived and it was seen that longer periods of therapy would be necessary. The patient had meanwhile begun to have fits which appeared to be controlled by intramuscular injections of magnesium sulphate. A.C.T.H. (Reiss) in a dose equivalent

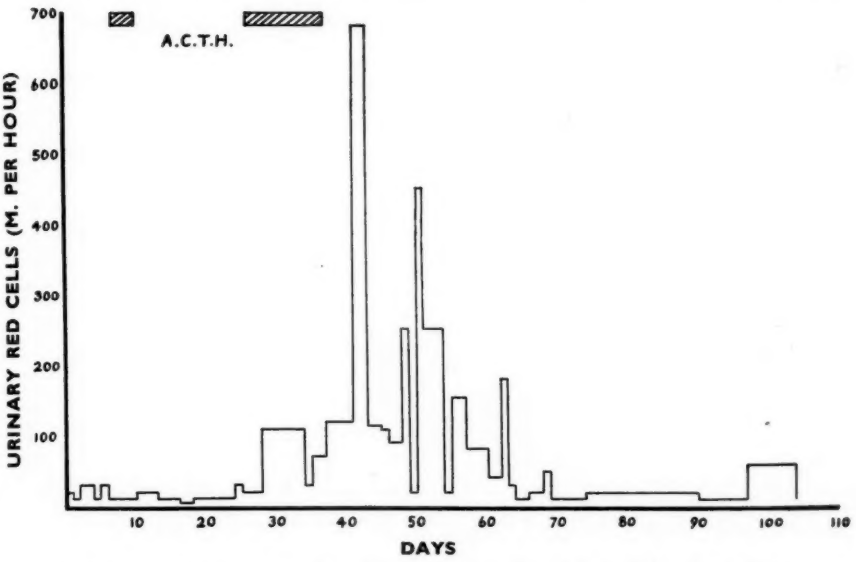

FIG. 1.—A.C.T.H. was administered on Days 7 to 10 inclusive and 26 to 37 inclusive.

to 25 mg. (Armour) six-hourly was given for 10 days. After a few days the haematuria increased and the blood pressure rose to 260/160 mm. Hg. However, the patient felt better, her sight seemed to improve and the papill-oedema to diminish. Two to three days after this course of A.C.T.H. there was a short rise in the haematuria to 680 million red cells per hour (during the control period the level had been about 5 million) but nevertheless a considerable sustained diuresis occurred, the patient passing off all the oedema, ascites and pleural effusions, and losing 36 lb. in weight in the course of 29 days. After a period of about five weeks the amount of urinary red blood cells had gradually reverted to the control levels (Fig. 1.)

In 1951 she was re-admitted to hospital because of an increase in haematuria following a sore throat. On admission the blood pressure was 140/100 mm. Hg, and the fundi showed evidence of secondary optic atrophy. The urine contained very many red cells and occasional granular casts. A throat swab grew β-haemolytic streptococci of Lancefield's group A, but after seven days' treatment with intramuscular penicillin further swabs remained repeatedly negative.

After a control period of 16 days cortisone was given intramuscularly in doses of 50 mg. three times a day. There was an immediate increase in the haematuria from approximately 100 million red cells per hour to 220 million red cells per hour. Cortisone was stopped on the seventh day and the haematuria fell to previous levels. After an interval of 12 days a further course lasting three weeks was given, and again there was an immediate sharp increase of haematuria but this soon fell to pre-treatment levels and ultimately below (Fig. 2).

Case 2.—A boy aged 9 years was first admitted to hospital in 1949 with the sudden onset of generalized oedema, proteinuria and numerous red cells and casts in the urine. After two months in hospital the oedema subsided, but proteinuria and haematuria were still present when he was discharged and persisted afterwards, so in April, 1951, he was re-admitted for a course of cortisone. On admission he looked well and there was no oedema. The blood pressure was 120/80 mm. Hg.

After a control period of 14 days he was given cortisone, 50 mg. three times a day by intramuscular injection, for five days. On the second day of treatment the haematuria increased from 800,000 red cells per hour to 2,000,000 red cells per hour and continued to rise.

At the same time the temperature rose to 101·4° F. and then continued at 99 to 100° F. until the fourth day of treatment. The throat was injected and culture revealed a profuse growth of group A β-haemolytic streptococci. In view of the possible harmful effect of cortisone in an infection it was stopped after five days. The haematuria rapidly fell to pre-treatment levels. Cortisone was withheld until the haematuria had become constant—a period of about two weeks. It was then again administered and once more there was an increase in haematuria, though not to such a degree as occurred in the first instance. The temperature rose to 100·4° F. on the third day and returned to normal on the fifth day. Cortisone was stopped on the sixth day. The throat culture was still positive for β-haemolytic streptococci. A further course of cortisone was given after 13 days when the haematuria had again settled to a constant level. Once again there was an increase of haematuria, but throat cultures had now become negative so cortisone was continued for 26 days. The haematuria rose once more this time to about 5 million red cells per hour and then gradually decreased throughout the rest of the cortisone course. The final level

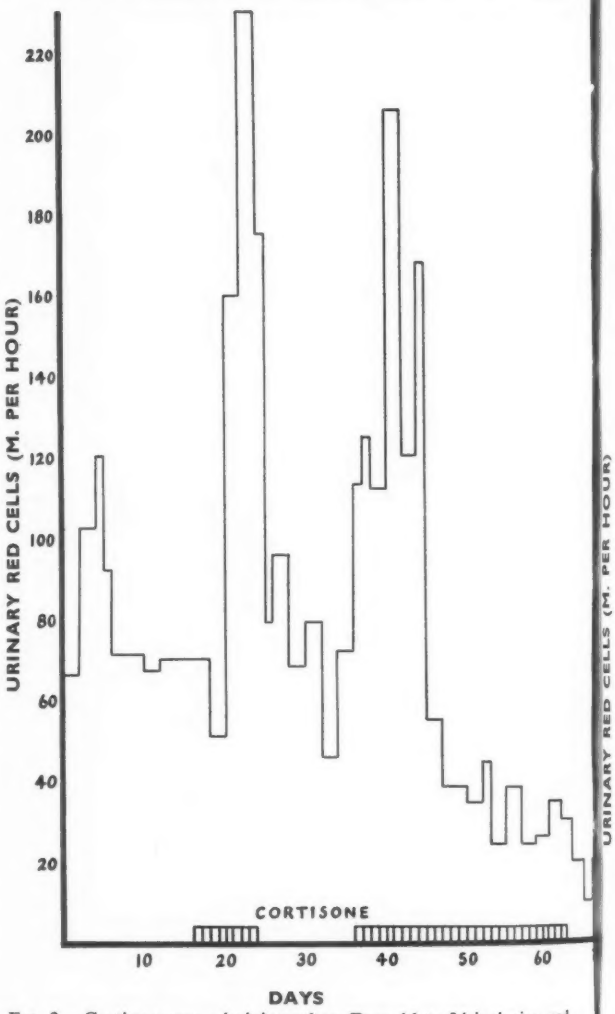

FIG. 2.—Cortisone was administered on Days 16 to 24 inclusive and 36 to 64 inclusive.

of 100,000 to 200,000 red cells per hour was lower than the initial level of 650,000 to 900,000 red cells per hour (Fig. 3).

Case 3.—A man aged 21 was seen in 1951 with a suspected salivary calculus which, however, was not confirmed radiologically. He stated that he had been rejected from the Armed Forces in 1950 for albuminuria. He had never had symptoms relating to the urinary system, but the urine was found to contain a large amount of protein, so he was admitted to hospital for investigation. He had no clinical oedema or any other abnormal physical signs. The blood pressure ranged from 140/90 to 170/90 mm.

Hg. The urinary deposit contained red cells, white cells and cellular casts. There was a little impairment in the urine concentration and an intravenous pyelogram showed good concentration. Investigation for renal tuberculosis, including microscopy and culture of urine from the bladder and ureters, proved negative. The blood cholesterol level was 330 mg. per 100 ml. Throat swabs taken on numerous occasions were all negative for β-haemolytic streptococci. Haemoglobin was 11·8 g. and the E.S.R. 38 mm. in one hour (Wintrobe).

After observations had been made on the red cell excretion over a period of about 20 days, he was given A.C.T.H., 25 mg. intramuscularly, four times a day for 19 days. The urine red cell count remained steady for seven days after which it rose very rapidly from 0·5 million to 17 millions per hour. When the A.C.T.H. was stopped the red cell excretion appeared to be already falling and it continued to fall until it reached the region of 2 million (Fig. 4).

Discussion

To these three cases of haemorrhagic nephritis progressing into a chronic phase cortisone or A.C.T.H. was given on seven separate occasions and on each occasion there was an increase in the haematuria. On each of the five occasions when cortisone was used the haematuria increased in from one to three days from the beginning of treatment. When A.C.T.H. was used the haematuria increased after eight days in Case 3 and immediately after beginning treatment in Case 1, though in the latter a much greater increase took place on the twelfth day after treatment had been stopped.

In Case 2 the first course of

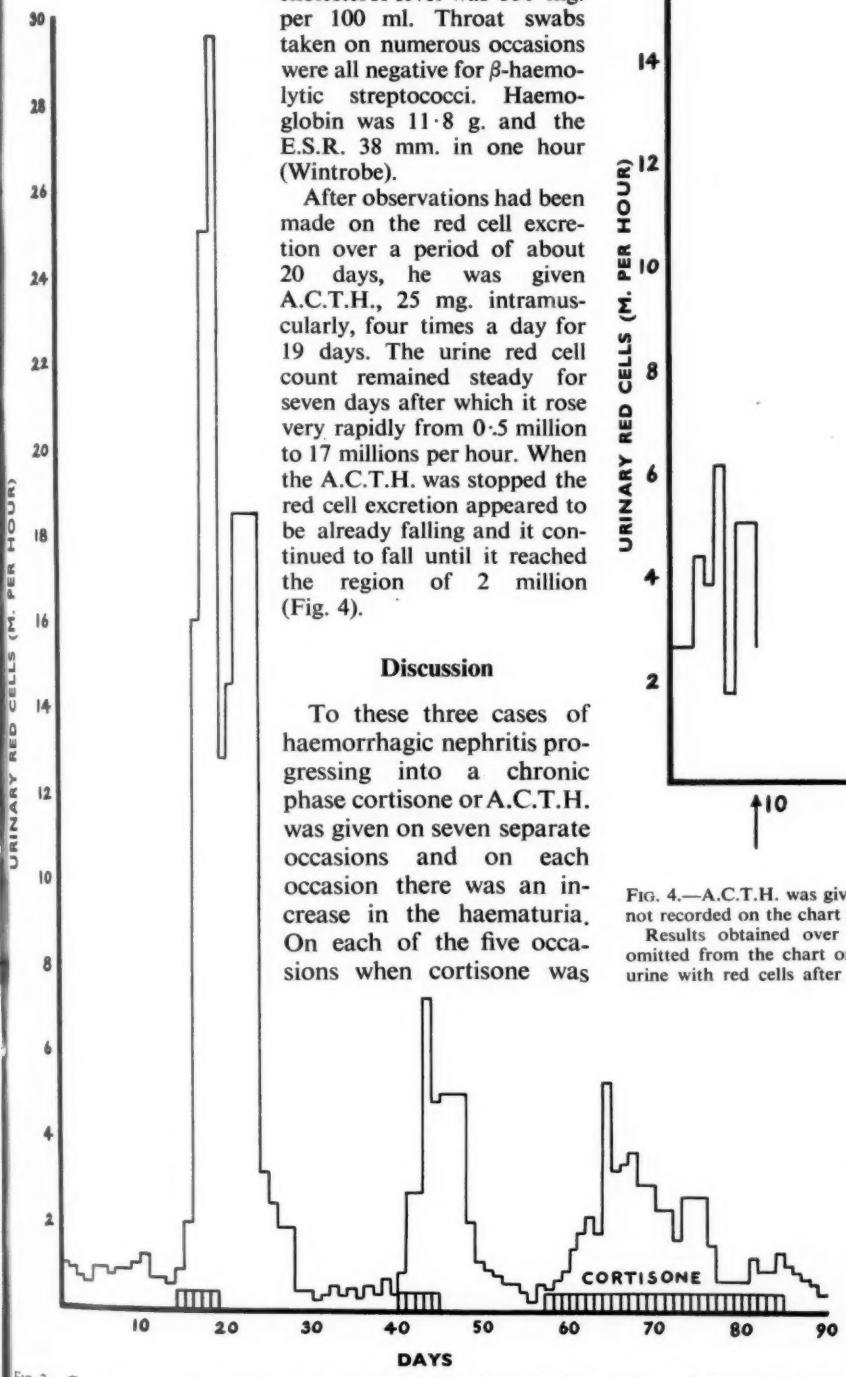

FIG. 3.—Cortisone was administered on Days 14 to 19 inclusive, 40 to 45 inclusive and 57 to 85 inclusive.

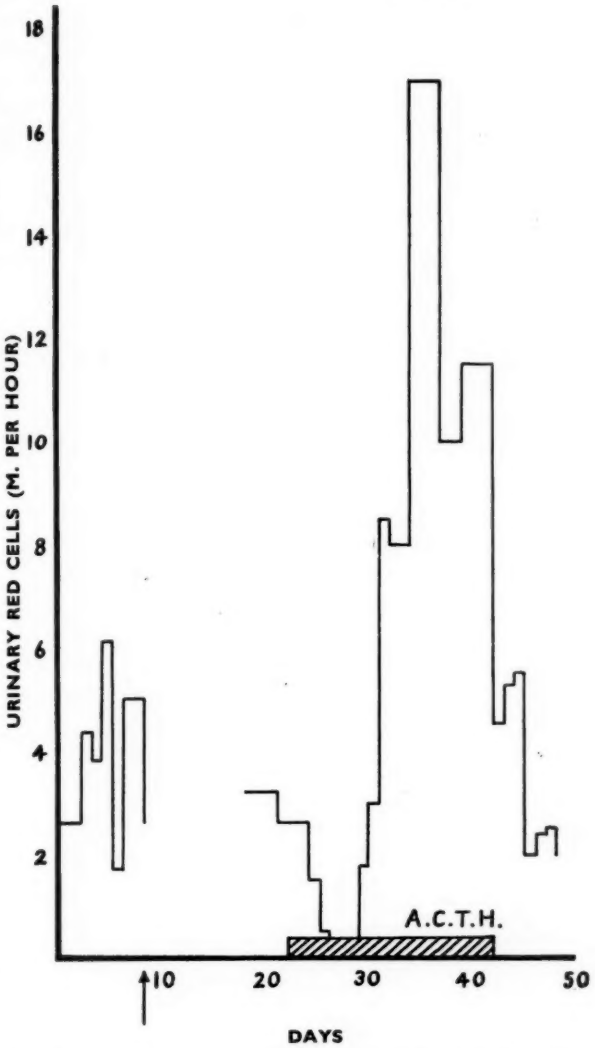

FIG. 4.—A.C.T.H. was given on Days 22 to 42 inclusive. Results are not recorded on the chart between Days 9 and 18 inclusive.

Results obtained over 10 days during the control period are omitted from the chart on account of heavy contamination of the urine with red cells after ureteric catheterization.

cortisone coincided with a streptococcal infection of the throat; in the second course, although scanty streptococci could still be grown, no increase in the number of colonies isolated took place nor was there any change in the appearance of the throat; in the third course of cortisone the haematuria increased although this time throat cultures were negative. It thus seemed more likely that the second and third exacerbations were due to a direct effect of cortisone on the kidney, rather than an indirect effect by stimulation of streptococcal inflammation in the throat. In the other cases the exacerbations all seemed to be related directly to cortisone or A.C.T.H.

The mechanism of this increased passage of red cells through the kidney during treatment of haemorrhagic nephritis with A.C.T.H. or cortisone is unknown.

Summary

Three courses of A.C.T.H. or cortisone were given in two cases of haemorrhagic nephritis, and one course of A.C.T.H. was given in a case of doubtful diagnosis but thought to be haemorrhagic nephritis.

In each patient there was a marked increase of haematuria, as measured by the urinary red cell count, every time the hormone was given. This increase took place in from one to eight days after treatment was begun.

We are grateful to Dr. G. A. Smart for suggesting this investigation and also for allowing us to publish reports on Cases 1 and 2 which were under his care. We are also glad to acknowledge Dr. J. E. Cates for his encouragement, advice and permission to publish Case 3.

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HYPERPYREXIA IN THE POST-KERNIKTERUS SYNDROME

BY

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Since Guthrie's description in 1914 it has been clear that if an infant survives the initial illness of icterus gravis neonatorum, and particularly if he has shown signs of neurological disturbance at the height of his jaundice, he is liable to suffer from permanent derangement of the central nervous system. Sobel and Zucker (1940) described the characteristic clinical tetralogy of choreoathetosis, extrapyramidal spasticity, opisthotonus and mental defect. This article describes further manifestations of the post-kernikterus syndrome occurring in seven infants. The main features were attacks of hyperpyrexia, sweating and head retraction without evidence of infection; in the majority the attacks were repeated many times, and, in all but one, death occurred during an attack. An eighth case occurred in an infant with acholuric jaundice, and in a ninth case the aetiology is uncertain. Four of the cases we have observed ourselves; for the details of the others we are indebted to the physicians who have given us access to their case records.

The nomenclature in this condition suffers from the fact that the term 'kernikterus' was originally limited to the naked-eye appearance of the nuclear masses. It is proposed in this article to limit the use of the word to its original meaning. The term 'clinical kernikterus' will be used to describe the original illness where a jaundiced infant shows the characteristic neurological signs, and the term 'post-kernikterus syndrome' for the cases of the survivors who show permanent changes.

Case Histories

Case 1. C.S. was the fifth child of normal parents. The siblings were normal. Delivery was normal at full term (birth weight 7½ lb.). The infant was normal at birth, but jaundice was noted within 24 hours. When admitted to hospital on the fourth day she was comatose, spastic and deeply jaundiced. She had grunting respirations and a temperature of 102° F. Haemoglobin was 100%. The infant was Rh positive (D positive). The direct Coombs test was positive. The mother was Rh negative (D negative). The Wassermann and Kahn tests were negative. The cerebrospinal fluid was xanthochromic.

The infant had several minor convulsions but settled with oxygen therapy. Over the next two weeks the haemoglobin fell to 58%, but the jaundice gradually cleared and her general condition improved. A transfusion of 120 ml. Rh-negative blood was given, and repeated after 11 days because of a further fall in haemoglobin.

The baby remained fairly well until the age of 4½ months, when she was readmitted with the story that she was constipated, refusing feeds, twitching and sweating. On admission she had a temperature of 102° F., pulse 150, respiration 50. She had head retraction which could be overcome with steady pressure. She was sweating violently. Nothing was discovered to account for the fever. The white cell count, urine and C.S.F. were normal.

Over the next three days the fever settled without specific treatment. It was noted that the head retraction continued after the temperature fell, and that she did not show the normal responses for her age.

From this time until her death at the age of 16½ months, she was readmitted to hospital 10 times. On each occasion she was pyrexial and head retraction was noted. Apart from one incident when there was a strong suspicion of otitis media no evidence of infection was ever discovered. She was usually constipated and, at the beginning of the attack, dyspnoeic, but the most notable feature of each attack was the profuse sweating. In the attacks her temperature usually remained between 101° and 102° F. without remission for three to four days, despite the use of a wide range of antibiotics in adequate dosage. Her temperature usually fell suddenly to normal; she would start taking feeds again and would be fit to return home in a few days.

Throughout the last 12 months of life there were intermittent bouts of generalized spasticity and twitching of the arms, and there were several major convulsions. There was no real mental progress. She continued to gain weight slowly and weighed 15 lb. just before her death in a typical attack. No necropsy was obtained.

Case 2. P.McC. suffered from icterus gravis neonatorum. During the initial illness he had head retraction.

At the age of 4½ months he was readmitted because of attacks of screaming and vomiting. He had a temperature of 104° F. and pulse of 160; his respirations were 48 per minute. He was spastic and there was head retraction; there were some generalized twitchings, and a few minor convulsions occurred. There was neither clinical nor laboratory evidence of infection, and the symptoms settled over the next few days without specific treatment. His mental development was retarded.

At the age of 7 months a similar attack occurred. He was admitted with a temperature of 105° F. and respiratory rate of 60. He was sweating profusely and there was marked constipation. This attack settled without evidence of infection and without specific treatment. During the next three months he remained in hospital and three more attacks were fully observed. At the age of 11 months he was readmitted in a similar state. He had several major convulsions and died within 48 hours. No evidence of infection was found at necropsy. On naked-eye examination the brain appeared normal; no histology was done.

Case 3. J.R. suffered from icterus gravis neonatorum and developed head retraction and a temperature of 106·8° F. on the third day of life. When she left hospital at the age of 3 weeks there was some general spasticity, and a minor degree of head retraction remained.

She was readmitted at the age of 10 weeks and again at 13 weeks with sudden attacks of crying and fever. Her temperature rose on each occasion to 104° F. and respirations to 50. There was profuse sweating and marked constipation, but there was neither clinical nor laboratory evidence of infection. She did not have normal responses for her age. At the age of 15 weeks she was admitted after a convulsion with a temperature of 102·5° F. and respirations of 64; she died the same day. At necropsy no evidence of infection was found. On naked-eye examination the brain appeared normal; no histology was done.

(A subsequent sibling who was also affected with haemolytic disease died in the neonatal period; classical kernikterus was demonstrated.)

Case 4. I.W. suffered from icterus gravis neonatorum and had marked head retraction from the fourth to the eighth day of life. He was readmitted to hospital at the age of 4½ months with retraction and fever. No evidence of infection was found, but he remained intermittently pyrexial—with a maximum of 106° F.—until he died eight days after admission. At necropsy the only positive finding was basal consolidation of the lungs. The brain appeared normal on naked-eye examination.

Case 5. M.S. suffered from icterus gravis neonatorum. An exchange transfusion was performed at the age of 12 hours. No neurological disturbances were noted in the neonatal period. At the age of 1 year it was noted that she showed marked mental retardation.

She was admitted to hospital at the age of 16 months after seven days of irritability and vomiting. Her temperature was 103° F.; there was marked head retraction and she was twitching. There was no evidence of infection. Her temperature rose to 107° F., and at this point she died. At necropsy the brain and meninges appeared congested and the C.S.F. was excessive. There was no evidence of infection.

Case 6. S.M. suffered from icterus gravis neonatorum. On the fifth day of life he had marked neck stiffness.

At the age of 4 months he was admitted with a history of vomiting. His temperature was 100·2° F. and soon rose to 106·8° F. There was hypertonicity and neck retraction; he had several convulsions. There was no evidence of infection, and he slowly settled, although he remained spastic. Five weeks later he had a further bout with a temperature of 105·4° F., violent sweating and convulsions. A week later he had his third typical bout but remains alive at the time of writing. He is spastic and apparently blind.

Case 7. P.J. was a week premature. He was not jaundiced in the neonatal period. His mother, however, noted that he always appeared to lie with his head pulled back.

He was reported to have made normal progress until the age of 4 months when he was admitted to hospital after three days' irritability, fever, vomiting and convulsions. He had head retraction and was generally spastic; he sweated violently and was very constipated; there was marked dyspnoea. He had a well marked plagiocephaly. There was no evidence of infection apart from a swollen gland in the neck. Over the next three months he was readmitted to hospital four times in a similar state. Air encephalograms showed slight general dilatation of the ventricles. He died in an attack with a temperature of 107·5° F. At necropsy there was no evidence of infection.

Case 8. A.McC. suffered from icterus gravis neonatorum. She was drowsy and had neck retraction for three days in the neonatal period.

At the age of 4 months she was readmitted with a history of vomiting. Her temperature rose to 105° F. and respirations to 60; she sweated violently. There was no evidence of infection. Three weeks later a further bout settled rapidly.

At the age of 8 months she was readmitted because of vomiting; her temperature rose to 105·6° F. She sweated violently and there was neck retraction. She died in a convulsion 24 hours later.

Case 9. C.G. suffered from acholuric jaundice. He became jaundiced on the third day of life and was drowsy for several days.

At the age of 5½ months, after a circumcision under general anaesthesia, he developed a temperature of 104° F. with rigidity of the lower limbs and neck. This settled in 48 hours but three days later his temperature rose to 105° F. and he was generally spastic. He settled without evidence of infection, but it was then noted that he did not show the normal responses for his age.

A month later he was admitted because of failure to make progress. After two days his temperature rose to 105° F. and he sweated violently. At this stage an air encephalogram showed moderate dilatation of the lateral ventricles. Three further bouts occurred over the next 12 days and in the last he died with a temperature of 105° F. At necropsy there was a moderate degree of ventricular dilatation. The lungs showed scattered areas

of consolidation but there was no other evidence of infection.

The course of the illness and the details of the attacks were remarkably similar in these nine infants. The attacks were sudden in onset and were sometimes ushered in by a convulsion. There was hyperpyrexia, tachypnoea and tachycardia. There was often a sweat rash during the acute episode, and in one case this went on to peeling of the hands and feet. Head retraction either appeared during the attacks or in some cases merely became more marked. The most striking feature in six cases was the sweating. During the attacks these infants were covered with beads of sweat; their clothes and pillows were soaked and they were extremely flushed. Intermittent convulsions were common. Until their terminal episodes most of the infants remained in a fair state of nutrition. It was remarkable how suddenly each attack subsided and how with a return to normal temperature the infants resumed what was for them normal behaviour.

In six of our cases the first recorded episode occurred between the age of 4 and 5 months. A 'silent period' after the neonatal jaundice was described in relation to other manifestations by Evans and Polani (1950), although in their cases the first clear symptoms usually appeared before the age of 3 months.

In many ways the episodes we have described were a recapitulation of the events which most of the infants had survived in the neonatal period.

The main findings are summarized in Table 1.

Special Features in Three Cases

There were certain special features in three of the cases which need further comment.

Case 7. The clinical syndrome was indistinguishable from that in the other eight cases. There was no evidence of Rhesus incompatibility. There was no history of neonatal jaundice, but the evidence about this period of his life is not clear. It seems possible that the central nervous system may have been subjected to the same influences which were associated with a more rapidly fatal outcome in the cases of kernikterus of prematurity described by Aidin, Corner and Tovey (1950) and Zuelzer and Mudgett (1950).

The brain in this case was subjected to a detailed examination. No histological changes could be demonstrated.

Case 8. The history and clinical picture in this case were typical of the majority of the series. This was the last patient in the series to die, and the brain was examined in the full awareness of the clinical syndrome. For the following report on the brain we are indebted to Dr. H. B. Marsden.

'BRAIN. There was marked congestion of the cortical vessels of the brain.

'Sections were taken through the pons, medulla, cerebellum, basal ganglia, frontal, temporal, parietal and occipital cortex and the hypothalamus. There was dilatation of the vessels throughout, this feature being most marked in the capillaries of the dentate nucleus. The vessel walls occasionally showed slight swelling with hyaline change. Small perivascular haemorrhages were readily noted and there was loss of structure in the tissues surrounding the vessels in some places. No "cuffs" were seen round the vessels but a perivascular glial focus and very rarely an isolated collection of small glial cells would be found. There was some eosinophilic swelling (on haematoxylin and eosin-stained sections) of the cytoplasm of glial cells although this was not a prominent feature. The neurons throughout had a swollen, indistinct appearance with poor staining qualities, although it was not possible to say how much of these changes was due to artefact.

TABLE 1
SUMMARY OF CHIEF CLINICAL FINDINGS

Case	1 C.S.	2 P.McC.	3 J.R.	4 I.W.	5 M.S.	6 S.M.	7 P.J.	8 A.McC.	9 C.G.
Clinical kernikterus	+	+	+	+	0	+	0	+	∓
Age (months at first episode)	4½	4½	2½	4½	16	4	4	4	5½
Age (months at death)	16½	11	3½	4¾	16	alive	7	8	7
No. of incidents	11	6	3	1	1	4	5	3	5
Sweating	+	+	+	0	0	+	+	+	0
Neck retraction	+	+	+	+	+	+	+	+	+
Convulsions	+	+	+	0	+	+	+	+	0
Mental and/or nervous changes between or before attacks	+	+	+	?	+	+	+	+	+
Highest recorded temperature (°F.)	102	105	106·8	106	107	106·8	107·5	105·6	105

'The changes in the basal ganglia and hypothalamus did not differ from those elsewhere. There was possibly some diminution of nerve cells in the basal ganglia although this could not be satisfactorily assessed. The nuclear masses in the hypothalamus, although showing evidence of small recent haemorrhages, were well represented.'

Case 9. This child came from a family known to suffer from acholuric jaundice. The grandfather and the mother both had had the spleens removed; an elder brother had had the spleen removed in childhood, and a subsequent sibling showed evidence of the disease in the neonatal period. In the latter infant a splenectomy was successfully performed at the age of 5 weeks.

In the patient C.S. jaundice appeared on the third day of life. The mother and child were both Rh positive and there were no maternal Rhesus antibodies. The spleen became palpable in the neonatal period and the red cell fragility both then and at the age of 6 months was abnormal. (Haemolysis began in 0·5% and was complete in 0·35% saline.)

In the neonatal period the picture of deep jaundice and drowsiness suggested clinical kernikterus. Before the baby died it was possible to observe the classical features of the post-kernikterus syndrome, as he was mentally retarded and showed athetotic movements. He was spastic, and the few teeth visible when he died showed definite discoloration although they were not recorded as being the usual green. Sections of the brain were examined in detail at a considerably later date, and for the following report we are indebted to Dr. H. B. Marsden.

'BRAIN. Many of the features seen in Case 8 were noted although haemorrhages were not seen and there was colloid material in the dilated perivascular spaces. Eosinophilic swelling of the cytoplasm of the glial cells was very noticeable. The capillary dilatation in the dentate nucleus was extreme. Adequate sections for full examination were not taken and there were no blocks from the hypothalamus. The appearances were regarded as being compatible with the effects of hyperpyrexia.'

Although acholuric jaundice has often been noted in the neonatal period there does not appear to be any previous description of its relation to kernikterus. The condition was mentioned by Evans and Polani (1950) only to exclude it as a possible cause.

Discussion

Previous descriptions of the post-kernikterus syndrome have drawn attention to lesions in the basal ganglia and hypothalamus. In mammalian temperature control the importance of the latter region is well established. Morgan (1938) and Morgan and Vonderahe (1939) suggested that the mammillo-infundibular nuclei were the most important centres. Disturbances of temperature control* might thus be expected as features of the syndrome and the tendency has been noted by several authors.

Zimmerman and Yannet (1935) described a child with the classical post-kernikterus syndrome who suffered from frequent attacks of pyrexia—with temperatures up to 106° F.—without evident cause. She died at the age of 3 years after having had a temperature of 102 to 106° F. almost continuously for the final five months. At necropsy there was no evidence of infection. There was a variable degree of destruction in the cellular elements of the basal ganglia, and special attention was drawn to the lesions in the mammillo-infundibular nuclei of the hypothalamic group.

Yannet and Lieberman (1946) reported a similar case, where the child died at the age of $3\frac{1}{2}$ years. At necropsy the changes were identical with those described by the previous authors.

Crigler and Najjar (1952) described the occurrence of kernikterus in a type of familial non-haemolytic jaundice. Out of seven children so affected four died during febrile episodes not apparently due to infection. Aidin, Corner and Tovey (1950) noted that hyperpyrexia was a common feature in the terminal stages of their cases of kernikterus in the premature infant.

Pyrexia of central origin is a well recognized phenomenon. Erickson (1939) described 20 fatal cases with varying lesions in the nuclear masses. The major features of the clinical syndrome were the absence of sweating and the coldness and pallor of the extremities, suggesting that there had been paralysis of the centres controlling heat loss. This picture contrasts markedly with that in our own cases where fever was accompanied by profuse sweating and flushing. We must explain this feature by postulating that the centres for heat loss were intact, but that the centres for heat production were in a state of intermittent excitement corresponding to the clinical episodes. It is impossible to state whether each episode was spontaneous, but it is possible that very minor disturbances or infections may have acted as a trigger on some occasions.

The occurrence of clear histological changes in every case would have helped to make the full picture of the syndrome clearer. Most of the cases were reviewed in retrospect, however, and the detailed material was not available.

We do not feel that this lack of histological confirmation invalidates the clinical concept.

* Since the completion of this article our attention has been drawn to the excellent review of kernikterus by Gerrard (*Brain*, 75, 526), where faulty temperature regulation is acknowledged as a frequent feature of the post-kernikterus syndrome.

Summary

A syndrome in infants is described where the main features were neck retraction, profuse sweating and hyperpyrexia of central origin.

Of nine cases described, eight were fatal. In eight there had been severe neonatal jaundice and of these six had shown definite evidence of nervous involvement ('clinical kernikterus') in the neonatal period.

Seven of the infants had suffered from haemolytic disease of the newborn.

One of the infants suffered from familial acholuric jaundice.

The possible mechanism of the disturbance is discussed.

We should like to thank the following physicians for permission to include details of cases under their care: Dr. Sylvia Guthrie, Dr. A. Holzel, Dr. R. I. MacKay, Dr. Margaret Egan, Dr. G. M. Komrower, Dr. M. L. Thomson and Dr. D. M. Anderson.

We are grateful to Professor W. F. Gaisford for advice and criticism and for permission to publish his cases, including in particular that of the infant with acholuric jaundice.

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HODGKIN'S DISEASE IN CHILDHOOD

BY

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All authorities agree that Hodgkin's disease is rare in childhood and extremely rare under the age of 7 years. The youngest patient in Hodgkin's (1832) original series was a boy of 10 years. Baker and Mann (1939) in a review of 65 cases admitted to Guy's Hospital, London, between the years 1920 and 1937 found seven children (10·8%) among them, the youngest being 7 years old. Charache (1946) in a review of the literature was able to find eight patients who had developed this disease under the age of 2½ years. The occurrence of a case of Hodgkin's disease first producing symptoms at the age of 1 year 9 months, and showing pathological features in the lungs not previously recorded in childhood was considered worthy of report.

Case Report

L.B., a boy aged 1 year 9 months, was admitted to the Royal Hospital for Sick Children, Edinburgh, on November 24, 1950, because of shortness of breath of several days' duration. He had been treated in the hospital a year earlier for infantile eczema and recurrent bronchitis, and both conditions had tended to improve slowly although he had a dry, flexural type of eczema and a dry, irritating cough at the time of his second admission. His respiratory rate was greatly increased to about 120 excursions per minute, but there was surprisingly little distress, no wheezing and no cyanosis; in fact the only abnormality detected on clinical examination of the respiratory system, apart from the tachypnoea, was the presence of a few medium crepitations at the bases of both lungs. Many rubbery nodes were noted in the axillae and groins, varying considerably in size, the largest being as big as a pigeon's egg and situated in the left groin. The edge of the liver was felt four fingerbreadths and the spleen two fingerbreadths below the costal margin (Fig. 1). His temperature was normal. A number of investigations were carried out, but only the more important ones are reported below.

Laboratory Studies. Haemoglobin (Sahli) was 95%, white cells, 11,600 (neutrophils 59%, lymphocytes 37%, monocytes 3%, eosinophils 1%) and platelets 440,000. The Mantoux test (1 in 100 dilution of O.T.) was negative. The serum calcium level was 10·5 mg.%, serum chlorides 646 mg.%, the plasma CO_2-combining power 60 volumes %, and a marrow smear was within normal limits. Radiographs of the skull, pelvis and long bones did not reveal any abnormality, but that of the chest showed a fine mottling throughout both lung fields suggestive of miliary tuberculosis or sarcoidosis.

A lymph node was removed from the left inguinal region for histological examination and this suggested the condition to be one of the malignant reticuloses. The picture was not typically that of Hodgkin's disease, but it was thought to be a variant of that condition.

FIG. 1.—L.B., aged 1 year 10 months, showing enlarged lymph nodes and enlarged liver and spleen.

In spite of treatment with nitrogen mustard (R 151 25 mg. b.d. for 33 days) his weight dropped steadily from 23 lb. to 19 lb., his general condition deteriorated, he developed what clinically appeared to be a fully fledged bronchopneumonia which did not respond to oxygen therapy and antibiotics, and he died on January 11, 1951, seven weeks after the onset.

Post-mortem Report. The cervical, axillary and inguinal lymph nodes were enlarged; most were approximately ½ cm. in diameter, firm, and had a homogeneous appearance on section, and a few were considerably larger. The trachea and bronchi were congested and there was a little mucopus in the lower trachea and major bronchi. The lungs were voluminous and the pleural surfaces were studded with emphysematous bullae, the largest being about ½ cm. in diameter. On section all the lung parenchyma seemed to be honeycombed by small emphysematous cavities and little normal tissue could be seen (Fig. 2). The bronchi stood out sharply from the surrounding tissue and some thin mucopus could be expressed from the cut ends. No evidence of infiltration of lung parenchyma could be found on macroscopic examination. The liver was very large and firm. It was

pale brown and on section was seen to be heavily studded with whitish deposits which suggested areas of cellular infiltration. Here and there the portal tracts had been severely infiltrated and as a result of biliary obstruction

FIG. 2.—Section of lung showing gross emphysema.

the infiltrated areas were locally stained with bile. The spleen was moderately enlarged and very firm. The capsule was wrinkled and on section the Malpighian bodies were very prominent. There was no obvious infiltration on macroscopical examination. Nothing of pathological interest was found in the brain, bowel, kidneys or elsewhere.

Histological Report. The pleura was healthy. The lungs showed tremendous emphysematous change. Many alveolar walls were broken down to form large air spaces. The bronchi were also affected and varying degrees of pathological change had occurred. In the most severely affected bronchi there was complete disorganization of the entire wall (Fig. 3). The epithelium had been stripped and the wall was replaced by Hodgkin tissue consisting of numerous reticulum cells with vesicular nuclei and pale acidophil cytoplasm. The cellular infiltration was remarkably isomorphic and no bizarre multinucleated forms of reticulum cells were seen. Here and there foci of eosinophil leucocytes were seen. The infiltrating tissue had spread longitudinally along the bronchovascular sheaths and had involved the adventitia of the pulmonary vessels. The arteries were involved slightly and only the adventitial coat was affected. The alveoli neighbouring the sites of bronchovascular infiltration showed interstitial infiltration with reticulum cells and eosinophils. In some areas the involvement of the peribronchial alveoli was very pronounced, their lumen being greatly reduced, and they appeared to be lined by prominent cuboidal cells thus giving a glandular appearance. Other bronchi had an almost intact epithelium but polypoid masses of Hodgkin's tissue were growing into the lumen (Fig. 4). The outer walls of these bronchi were also infiltrated. Still other bronchi showed squamous metaplasia of their lining epithelium and their lumen contained an acute inflammatory exudate with numerous polymorphonuclear leucocytes and cellular debris. This was probably the result of an acute terminal infection. The

FIG. 3.—Large bronchus × 12 (haematoxylin and eosin). The bronchial wall has been replaced by Hodgkin tissue.

appearances in the lungs were those of Hodgkin's disease of the bronchovascular infiltrative type. The results of this extensive bronchovascular, interstitial and intrabronchial infiltration had been a chronic partial obstruc-

tion of the air passages and the development of severe emphysema (Fig. 5).

The capsule of the liver was normal. The liver cells were healthy and the lobular pattern was preserved. The portal tracts showed moderate infiltration with reticulum cells and eosinophil cells. There was a considerable increase in the fibrous tissue of the portal tracts and fibroblastic activity was still present. The bile ducts were healthy. The portal tracts were extending out into the parenchyma and there was proliferation of small bile

FIG. 4.—Lung × 35 (haematoxylin and eosin). Hodgkin tissue is growing into the bronchial lumen causing partial obstruction.

ducts at the periphery of the larger portal tracts. The appearance was that of an early cirrhosis, with fibrous tissue proliferation a more prominent feature than cellular infiltration. In one section there was a large portal tract with greatly increased fibrous tissue and proliferation of small bile ducts. In the centre of the fibrous tissue was a large circular area of Hodgkin's tissue surrounded by a capsule of fibrous tissue. Numerous reticulum cells with pyknotic nuclei and abundant pale acidophil cytoplasm were present near the central area which was necrotic. The lesion might have undergone necrosis as a result of the use of nitrogen mustard but had been too large to undergo replacement fibrosis.

In the spleen the pulp was congested. The Malpighian bodies showed reticulum cell proliferation in their germinal centres but there was surprisingly little upset in the architecture of the organ.

The capsule of an inguinal lymph node was thickened. The structure was partly replaced by Hodgkin tissue. This consisted of a proliferative lesion of reticulum cells with numerous giant cells of the Greenfield type and some eosinophil cells (Fig. 6). There were small areas of necrosis and a generalized increase in the fibrous tissue

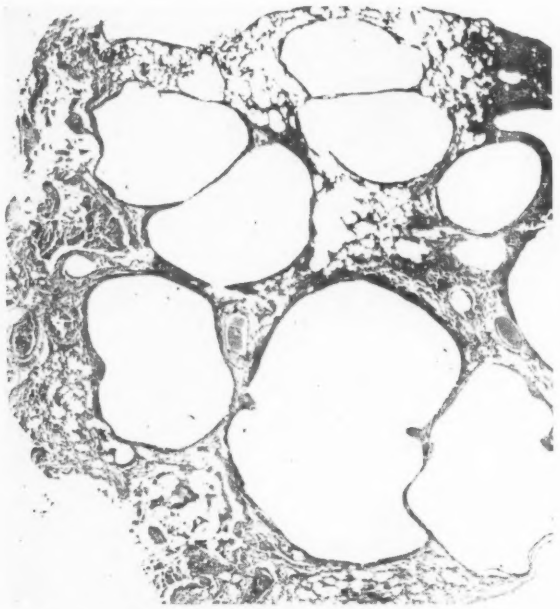

FIG. 5.—Lung × 8 (haematoxylin and eosin). Honeycomb appearance of lung resulting from gross emphysema.

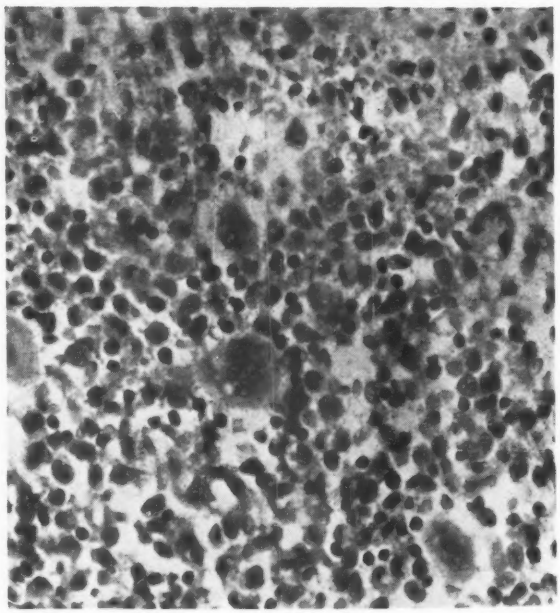

FIG. 6.—Lymph node × 350 (azoeosin). Numerous giant cells and eosinophil leucocytes are seen.

framework. Similar changes were found in mediastinal, mesenteric, Peyer's patches and other lymph nodes.

The kidneys, pancreas and heart showed nothing of pathological interest.

Discussion

The reticuloses are an important group of disorders in infancy and childhood. They comprise the leukaemias, Hodgkin's disease, the lipoidoses, the non-lipoid reticuloses such as Letterer-Siwe disease and familial haemophagocytic reticulosis, and the reticulosarcomata. The leukaemias and the lipoidoses are relatively easily differentiated from Hodgkin's disease but the other forms may cause some difficulty, especially in infants. Letterer-Siwe disease, haemophagocytic reticulosis and Hodgkin's disease may all present with generalized painless enlargement of the superficial lymph nodes and intermittent fever. In both Letterer-Siwe disease and in the intrapulmonary form of Hodgkin's disease x-ray examination of the chest shows a fine mottling reminiscent of miliary tuberculosis or sarcoidosis. The reticulosarcomata are generally confined to one group of lymph nodes but affection of the cervical group is common both in Hodgkin's disease and reticulosarcoma.

Final diagnosis rests with the histological findings in a biopsy specimen. Cervical nodes are more suitable than inguinal nodes for this type of examination on account of the frequency of non-specific changes in the latter.

Intrathoracic lesions are common in Hodgkin's disease, and at necropsy the mediastinal lymph nodes are almost invariably involved. This glandular enlargement may cause collapse of the lung from pressure effects or the disease process may extend from the hilar glands into the lung parenchyma directly or via the peribronchial and perivascular lymphatics. A more rare type of lesion is a granulomatous bronchitis and peribronchitis as was seen in our case. This type of lesion has been described by Moolten (1934) in an adolescent but does not seem to have been reported previously in an infant. In this form the bronchi are replaced by Hodgkin tissue composed of reticulum cells, giant cells, eosinophils and lymphocytes. The disease process spreads along the bronchovascular spaces, papilliform outgrowths of Hodgkin tissue project into the bronchial lumen and tend to cause obstruction of the air passages and gross emphysema may develop. This occurred in the present case. Hodgkin pneumonia caused by infiltration of Hodgkin tissue throughout the lung alveoli has also been described (Moolten, 1934). Occasionally plaques of Hodgkin tissue are found on the visceral pleura and a serosanguineous effusion develops. Schwind and Hyde (1942) have reported the occurrence of Hodgkin's disease in an infant. In their case there was a plaque of Hodgkin tissue on the surface of both lungs and Hodgkin tissue was also found in the lung parenchyma. The abdominal organs and retroperitoneal lymph nodes were also extensively involved. Schwind and Hyde were able to find only eight previously reported causes of Hodgkin's disease in infants. Of these eight cases, three were congenital, three showed involvement of the cervical glands and two of the thymus.

Summary

A case of Hodgkin's disease occurring in a child of 1 year and 9 months is described. Granulomatous bronchitis and peribronchitis was found at necropsy. This rare lesion has not previously been reported in childhood.

We are grateful to Professor J. L. Henderson for giving his permission to publish this case.

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SOME SOCIAL AND ETHNIC VARIATIONS IN THE PHYSIQUE OF SOUTH AFRICAN NURSERY SCHOOL CHILDREN

BY

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Physical growth in children is a basic physiological process. Although growth is easily measured it is relatively infrequently used in the assessment of the well-being of the individual child. Stuart (1943) and Washburn (1950) have effectively put the case for studying growth of children and using bodily measurements as a routine in the clinical examination of children. It is therefore important to collect and analyse the basic data with which a child can be compared in the consulting room.

However, the limitations of the use of such standards must also be remembered. In a malnourished community the mean scores will be below optimal scores and attainment of the average or above average scores would give no automatic cause for satisfaction. Care must also be taken not to use the attained size of a child as the only index of its nutritional state. Very serious nutritional upsets, e.g. pellagra or scurvy, may occur in well covered children, and the development of oedema will of course give the weight of the child an entirely different meaning. Thus the physique of the child must be regarded as only a part of the clinical examination and must be taken in conjunction with the state of the individual tissues before assessing nutrition. In other words both quality and quantity of the tissues are important.

The rate of growth is considered more valuable than the attained size at a given age because 'growth is a form of motion' (Tanner, 1952) but such standards are more difficult to come by and have so far not been widely used. Serial measurements of a child are of greater value than single measurements because a big child may lose a considerable amount of weight and still be above the average for his age.

In these days of respect for mathematical exactitude it is important too to remember that there is a range of 'normal'. The use of the standard deviation with the mean will give the distribution of the scores in the particular group around that mean, provided the distribution is normal. Thus the mean ± 1 S.D. will include 68% and the mean 2 S.D. will include 95% of the group.

Another important use for somatometric standards is as an ancillary for the assessment of a community's health. Standards have been found to change temporally and have increased in countries such as the U.S.A. (Meredith, 1941), while in wartime Europe the standards with some exceptions dropped (Keys, Brožek, Henschel, Mickelsen and Taylor, 1950). Body size varies too with social and economic status, but ethnic influences have been difficult to separate from environmental factors (Meredith, 1941).

In South Africa little attention has been devoted to the study of the growth of children, and in the nursery school age group (2 to 6 years) only two published studies could be found (Woodrow and Robertson, 1950; Robertson, 1952). The present study has been undertaken with the object of remedying this deficiency and of stimulating the interest of paediatricians, nursery school workers and others interested in child welfare.

The data used in this study have been extracted from the records of 11 South African nursery schools and were divided into three groups:

1. White Upper-Income Group. These were children of professional, industrialist or managerial classes.

2. White Lower-Income Group. These were children from poorer suburbs whose parents were municipal and tramway workers, unskilled labourers, unemployed, etc.

3. Bantu Group. These were children living on a native sub-economic housing estate whose parents ranged from teachers and clerks to unskilled labourers. On the whole these children came from the better-off homes in an above-average urban native community. Nevertheless these children almost invariably showed signs of malnutrition when

the skin and mucous membrane were examined. They were considerably superior in height and weight to a similar group of Bantu pre-school children near Pretoria reported by Robertson (1952).

The children were all weighed and measured at the nursery schools by members of their respective staffs in the mornings. In two of the schools (upper-income group nursery school and the Bantu nursery school) the children were weighed in the nude. In the remaining schools the children wore underclothes or light indoor clothes only. In all schools the scales were tested with a periodicity ranging from monthly to twice yearly.

Heights were measured with the child standing erect barefoot against a wall in nine of the 11 schools. In the two remaining schools (one upper-income group and one lower-income group) the child stood erect on the platform of a scale which was fitted with a vertical measuring rod and a horizontal arm which rested on the head.

Although there was no close uniformity in the methods used in the different schools it was apparent that serious attempts were made to make the measurements as accurate as the method used allowed.

The sources of the figures analysed are shown in Table 1. Thus there were 392 boys and 409 girls who were weighed 4,717 times and had their heights measured 4,302 times between the ages of $2\frac{1}{4}$ and $6\frac{1}{4}$ years of age. Not more than one measurement each for height and weight for each quarter year of each child's age were used in the analysis that follows.

TABLE 1
DATA CONCERNING THE FIGURES USED FOR ANALYSIS

	Upper-Income Group		Lower-Income Group		Bantu Group	
	Boys	Girls	Boys	Girls	Boys	Girls
No. of children	143	115	140	176	109	118
No. of measurements of weight	578	543	1,070	1,101	663	762
Average no. of weights per child	4·04	4·72	7·64	6·26	6·08	6·46
No. of measurements of height	526	513	1,070	1,097	495	601
Average no. of heights per child	3·68	4·46	7·64	6·23	4·54	5·09
Durban nursery schools Period of Survey	1 (1943-1947)		—		1 (1947-1951)	
Johannesburg nursery schools Period of Survey	3 (1946-1948)		5 (1936-1946)		—	
Capetown nursery schools Period of Survey	1 (1946-1949)		—		—	

Findings and Discussion

The findings for boys and girls in the three groups are shown in Tables 2 and 3.

Difference between the Sexes. Most authors giving heights and weights for pre-school children separate the sexes (Greenwood, 1913; Peatman and Higgons, 1938; Kincaid and Stuckey, 1938; Gore and Palmer, 1949; Simmons, 1944; Mitchell and Nelson, 1945; Robertson, 1952). A few have not done so (Sheldon, 1943; Woodrow and Robertson, 1950). In those cases where the sexes have been separated the boys have usually been taller and heavier than the girls over the period from 2 to 6 years with the tendency for the differences to lessen towards the end of the period. The study published by Robertson (1952) was exceptional. His heights and weights were those of Bantu pre-school children attending a crêche near Pretoria and on the whole his girls were taller and heavier than his boys.

Table 4 summarizes the sex differences found in the present study.

It can be seen that the upper-income group children roughly followed the pattern usually found and the boys were generally heavier and taller than the girls. The lower-income group boys were generally heavier than girls of the corresponding ages, but after the age of $3\frac{1}{2}$ years the girls were nearly always superior in height. However, the superiorities in height of the girls were small in most cases and the average superiority in height amounted to only 0·03 inches over the 17 ages used for comparison.

In the Bantu group the boys were generally inferior in weight, but slightly superior in height so that the girls were more stockily built. None of the individual comparisons gave a difference which was statistically significant.

As far as we are aware little Bantu girls in this particular community receive no treatment which would account for their unusual weight superiority over the boys. It is, however, interesting to note that Kark (1952), in discussing the stature and weight of Bantu school children in the Pholela Native Reserve, concludes that 'when compared with other boys and girls (Pretoria European, British and American of various racial and ethnic groups) it would seem that Pholela boys are somewhat more retarded in stature and weight than are the Pholela girls'. In this group of school children the boys showed a higher incidence of clinical signs of malnutrition than the girls.

Obviously further investigation of bigger samples is required to confirm or refute the results of this study. The child-rearing techniques used in Bantu families should also be investigated in case there are factors which produce heavier girls than boys.

Comparison of the Groups. The upper-income group boys were found to be heavier and taller than lower-income group boys of the corresponding ages. The differences were 3 to 5 lb. in weight and 2 to 2¼ in. in height. These differences were all significant in each age group from 2¾ to 5½ years.

The upper-income group girls were consistently heavier and taller than the lower income group girls of the corresponding ages. The differences were 2 to 4½ lb. and 1¼ to 2½ in. These differences were all significant in each age group from 2½ to 5¼ years.

The lower-income group boys' weights were higher

TABLE 2
WEIGHTS OF SOUTH AFRICAN NURSERY SCHOOL CHILDREN

Age (years)	White Upper-Income Group			White Lower-Income Group			Bantu Group		
	No.	Mean (lb.)	S.D.	No.	Mean (lb.)	S.D.	No.	Mean (lb.)	S.D.
(a) Boys									
2¼				25	26·92	2·97			
2½	18	32·11	—	35	28·17	2·52			
2¾	31	33·73	3·82	37	29·58	2·81	16	29·12	—
3	37	33·63	3·71	50	30·82	2·68	19	29·66	—
3¼	55	35·35	4·18	53	31·51	2·81	36	31·50	3·50
3½	57	36·60	4·22	63	32·94	3·42	43	33·22	3·99
3¾	60	37·35	3·87	69	33·92	3·26	45	33·72	3·81
4	52	38·10	3·78	70	35·14	3·51	54	34·70	3·64
4¼	61	39·73	3·50	80	35·87	3·72	52	35·32	3·16
4½	61	40·91	4·18	90	37·00	3·86	56	36·41	3·42
4¾	45	42·30	4·64	95	37·77	3·82	55	37·25	3·85
5	40	43·02	4·73	95	39·06	4·08	52	38·62	4·17
5¼	41	43·79	4·93	84	40·01	4·02	55	39·25	4·21
5½	20	46·40	5·99	79	41·42	4·28	58	39·81	4·74
5¾				66	42·85	4·47	55	41·05	4·77
6				52	43·71	4·69	43	42·41	4·92
6¼				27	44·13	4·64	24	43·00	4·62
(b) Girls									
2¼				26	25·3	2·49			
2½	22	30·91	3·10	39	27·42	2·80			
2¾	28	30·89	3·54	49	28·50	3·16	20	29·70	3·39
3	35	32·36	3·07	59	30·11	3·57	24	30·92	3·17
3¼	38	34·18	3·95	68	31·07	3·48	38	31·24	3·32
3½	44	34·89	3·96	64	32·61	3·46	44	33·20	3·53
3¾	66	36·38	3·96	79	33·21	3·67	51	33·87	3·43
4	65	36·65	4·46	86	34·85	3·41	57	34·50	4·45
4¼	49	38·68	4·01	91	35·92	3·90	62	35·63	4·16
4½	42	41·62	5·23	88	36·77	4·02	71	36·68	4·12
4¾	55	42·19	5·21	82	37·83	3·97	69	37·38	4·35
5	48	42·54	4·78	83	38·84	3·74	64	38·69	4·48
5¼	33	44·32	5·96	82	39·92	4·40	66	40·76	5·63
5½	18	43·78	—	75	41·27	4·33	65	40·96	5·42
5¾				66	41·56	4·03	60	41·70	5·39
6				40	43·33	3·91	42	42·12	5·52
6¼				24	43·58	4·93	29	43·71	5·68

(with one exception) than those of the Bantu boys, the differences being 1·8 lb. or less. Only in the $5\frac{3}{4}$ age group was the difference (1·8 lb.) significant. The lower-income group boys' heights were greater than those of Bantu boys by 0·26 to 1·35 in. Between $3\frac{1}{4}$ and 6 years of age the differences were significant at $4\frac{1}{4}$, $4\frac{1}{2}$, $4\frac{3}{4}$, $5\frac{1}{2}$, $5\frac{3}{4}$ and 6 years.

The lower income group girls were heavier than the Bantu girls in seven out of 15 age groups. The difference in the various age groups ranged from 1·2 lb. to —1·2 lb. and none of the differences was significant.

TABLE 3
HEIGHTS OF SOUTH AFRICAN NURSERY SCHOOL CHILDREN

Age (years)	White Upper-Income Group			White Lower-Income Group			Bantu Group		
	No.	Mean (lb.)	S.D.	No.	Mean (in.)	S.D.	No.	Mean (in.)	S.D.
(a) Boys									
$2\frac{1}{4}$				25	33·37	1·44			
$2\frac{1}{2}$	15	36·58	—	35	34·30	1·38			
$2\frac{3}{4}$	28	37·39	2·10	37	35·30	1·24			
3	34	38·13	1·30	50	36·14	1·14	16	34·94	—
$3\frac{1}{4}$	47	39·07	1·82	53	36·89	1·31	27	36·36	2·26
$3\frac{1}{2}$	55	39·64	1·46	63	37·42	1·38	34	37·16	1·97
$3\frac{3}{4}$	53	40·41	1·48	69	38·07	1·47	32	37·47	1·69
4	45	41·01	1·31	70	38·87	1·51	41	38·33	2·06
$4\frac{1}{4}$	57	41·70	1·27	80	39·45	1·58	43	38·73	1·48
$4\frac{1}{2}$	59	42·44	1·36	90	40·13	1·72	41	39·13	1·68
$4\frac{3}{4}$	37	42·82	1·82	95	40·82	1·76	44	40·11	1·45
5	41	43·59	1·74	95	41·54	1·80	40	40·80	2·07
$5\frac{1}{4}$	39	44·22	1·63	84	42·11	1·79	42	41·50	2·02
$5\frac{1}{2}$	16	44·99	—	79	42·92	1·68	44	41·99	1·92
$5\frac{3}{4}$				66	43·78	1·66	41	42·64	1·64
6				52	44·34	1·70	33	42·99	1·79
$6\frac{1}{4}$				27	44·49	1·58	17	43·60	—
(b) Girls									
$2\frac{1}{4}$				25	33·09	1·56			
$2\frac{1}{2}$	22	36·34	1·03	38	33·91	1·27			
$2\frac{3}{4}$	26	37·46	1·37	48	34·76	1·37	17	34·25	—
3	34	37·85	1·31	58	36·02	1·59	13	34·98	—
$3\frac{1}{4}$	35	38·89	1·78	68	36·76	1·76	32	35·10	1·60
$3\frac{1}{2}$	40	39·30	1·53	64	37·42	1·53	30	36·57	1·89
$3\frac{3}{4}$	64	40·08	1·48	84	38·19	1·58	43	37·06	1·76
4	60	40·73	1·52	85	39·05	1·66	39	38·10	2·10
$4\frac{1}{4}$	48	41·56	1·26	90	39·72	1·78	47	38·72	1·71
$4\frac{1}{2}$	42	42·62	1·49	87	40·22	1·69	51	39·58	1·67
$4\frac{3}{4}$	47	42·91	1·46	82	41·12	1·60	56	40·03	1·73
5	47	43·46	1·54	81	41·80	1·74	53	40·58	1·75
$5\frac{1}{4}$	33	43·92	1·77	84	42·65	1·66	50	41·92	1·49
$5\frac{1}{2}$	15	44·48	—	74	43·13	1·87	59	42·17	1·98
$5\frac{3}{4}$				66	43·67	1·84	48	42·50	1·74
6				39	44·42	2·37	36	42·79	2·04
$6\frac{1}{4}$				24	44·58	1·44	27	43·86	1·91

TABLE 4
SEX DIFFERENCES IN WEIGHT AND HEIGHT OF NURSERY SCHOOL CHILDREN*

Ages	Upper-Income Group		Lower-Income Group		Bantu Group	
	Weights (lb.)	Heights (in.)	Weights (lb.)	Heights (in.)	Weights (lb.)	Heights (in.)
2¼			+1·19	+·28		
2½	+1·20	+·21	+0·75	+·39		
2¾	+2·84	−·07	+1·08	+·54	−·58	
3	+1·27	+·28	+0·71	+·12	−1·26	−·04
3¼	+1·17	+·18	+0·44	+·13	+·26	+1·26
3½	+1·71	+·34	+0·33	0	+·02	+·59
3¾	+0·97	+·33	+0·71	−·12	−·15	+·41
4	+1·45	+·28	+0·29	−·18	+·20	+·23
4¼	+1·05	+·14	−0·05	−·27	−·31	+·01
4½	−0·71	−·18	+0·23	−·09	−·27	−·45
4¾	+0·11	−·09	−·16	−·30	−·13	+·08
5	+0·48	+·13	+·22	−·26	−·07	+·22
5¼	−0·56	+·30	+·09	−·54	−1·51	−·42
5½	+2·62	+·51	+·15	−·21	−1·15	−·18
5¾			+1·29	+·11	−·65	+·14
6			+·38	−·08	+·29	+·20
6¼			+·52	−·09	−·71	−·26
Average	+1·04	+·18	+·48	−·03	−·40	+·13

* + sign indicates boys superior. − sign indicates girls superior.

The lower-income group girls were taller than the Bantu girls by 0·72 to 1·66 in. in the age groups 3¼ to 6¼ years. All the differences were significant except at 6 and 6¼ years.

It follows that the upper-income group children were heavier and taller than the Bantu children of the corresponding sex and age groups. Wherever a comparison could be made the differences were found to be significant.

On the whole it can be stated that: (1) Upper-income group boys and girls were three-quarters of a year in advance of lower-income group boys and girls respectively both in weight and in height. (2) Lower-income group boys were equal to or up to a quarter of a year in advance of Bantu boys in weight and about a quarter of a year in advance in height. (3) Lower-income group girls were about equal to Bantu girls in weight and about a quarter of a year in advance in height. It seems therefore that the economic group to which a child belongs is more powerful in determining the size of the nursery school age child than the ethnic group.

Comparison with Other Studies. It is interesting to compare the heights and weights of our two samples of white children with those obtained in other countries. Tables 5a and 5b show the figures obtained in the present series compared with studies in America, Australia and England.

Study of these figures reveals that the South African upper-income group children are equal or slightly superior to two superior groups of American children with regard to weight and height. On the other hand, the South African lower-income group children were lighter and shorter than children of similar economic groups in London and Melbourne.

The heights and weights given by Woodrow and Robertson (1950) for Cape Town children cannot easily be brought into this comparison because the sexes have been combined in their series. In general, however, their weights and heights for white (European) children fall between those of the upper-income and the lower-income groups. Their coloured* (non-European) children are 2 to 7 lb. lighter than the Bantu groups while their heights are approximately the same so that their children must be more slender in build.

It must be emphasized that comparisons between different studies must be accepted with caution because of the absence of uniformity of methods of measurement.

Summary

The uses and limitations of somatometric tables for height and weight are discussed as measures of individual and of group health.

The heights and weights of 392 boys and 409 girls attending 11 South African nursery schools have been divided into three groups, viz., white upper-income group, white lower-income group and Bantu group.

Analysis of these measurements reveals the following main findings: (*a*) The upper-income group boys are taller and heavier than upper-income group girls of the same ages. (*b*) The lower-income group boys are heavier but slightly shorter on the whole than lower-income group girls. (*c*) The Bantu boys are lighter but taller on the whole than Bantu girls. (None of these differences between the sexes in each class was significant.) (*d*) The upper-income group boys were significantly heavier and taller than the lower income group and the Bantu boys. (*e*) The upper-income group girls were significantly heavier and taller than the lower-income group and the Bantu girls. (*f*) The lower-income group boys were usually heavier and taller than the Bantu boys, the weight differences being significant at one age only, and the height differences significant at most ages after 4¼ years. (*g*) The lower-income group girls were approximately the same weight as the Bantu girls,

* 'Coloured' consists of a mixed group derived from White, Malay, Bantu, Hottentot and other ethnic groups.

TABLE 5

COMPARISON OF PRESENT SERIES WITH RESULTS IN OTHER COUNTRIES*

Age	South Africa (1)*	U.S. America (2)	U.S. America (3)	Australia (4)	England (5)	South Africa (6)	South Africa (1)	U.S. America (2)	U.S. America (3)	Australia (4)	England (5)	South Africa (6)
	(a) Weights (lb.)		BOYS						GIRLS			
2½	32·11	31·39	30·8	30·25	30·78	28·17	30·91	30·09	29·4	29·06	29·46	27·42
3	33·63	33·53	33·8	32·56	32·81	30·82	32·36	32·43	31·8	31·06	31·55	30·11
3½	36·60	35·85	35·9	34·43	34·66	32·94	34·89	34·94	32·6	32·75	33·59	32·61
4	38·10	38·40	38·1	36·50	36·64	35·14	36·65	37·06	36·7	35·69	35·58	34·85
4½	40·91	40·46	41·0	39·06	38·61	37·00	41·62	40·03	38·6	37·75	37·58	36·77
5	43·02	42·79	41·4	42·31	40·59	39·06	42·54	42·16	41·4	41·19	39·59	38·84
5½	46·40					41·42	43·78					41·27
6		48·22				43·71		48·26				43·33
	(b) Heights (in.)		BOYS						GIRLS			
2½	36·58	36·31	36·4	35·14		34·30	36·34	35·87	35·8	35·14		33·91
2¾					35·8						35·2	
3	38·13	37·94	38·3	36·58		36·14	37·85	37·55	37·4	36·58		36·02
3¼					37·6						36·8	
3½	39·64	39·49	39·5	37·95		37·42	39·30	39·18	38·9	37·95		37·42
3¾					38·9						38·7	
4	41·01	40·95	41·1	39·23		38·87	40·73	40·67	40·6	39·23		39·05
4¼					39·9						39·3	
4½	42·44	42·38	42·7	40·45		40·13	42·62	42·17	41·9	40·45		40·22
4¾					40·9						40·6	
5	43·59	43·57	43·5	41·78		41·54	43·46	43·54	43·4	41·78		41·80
5¼												
5½	44·99					42·92	44·48					43·13
6		46·34				44·34		46·31				44·42

* (1) Present series, upper-income group white children from three South African cities 1943-1949. (2) Simmons (1944) children of above average parents economically and educationally in Cleveland, U.S.A., 1932-1942. (3) Peatman and Higgons (1938) middle and well-to-do classes children having optimal home and paediatric care in New York (no period stated). (4) Kincaid and Stuckey (1938) children 'with no defects' from poorer classes in Melbourne (no period stated). (5) Gore and Palmer (1949) children attending L.C.C. clinics in London, 1947. (6) Present series, lower-income group white children from Johannesburg (1936-1946).

but the former were taller (significantly so at most ages) than the latter.

The heights and weights of the South African children are compared with those recently obtained in other countries. The upper-income group children are superior or equal to the best overseas standards. The lower-income group and Bantu are inferior to the worst of these standards.

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A HISTORY OF INFANT FEEDING

BY

IAN G. WICKES

PART II. SEVENTEENTH AND EIGHTEENTH CENTURIES

(RECEIVED FOR PUBLICATION FEBRUARY 5, 1953)

Seventeenth Century Writers

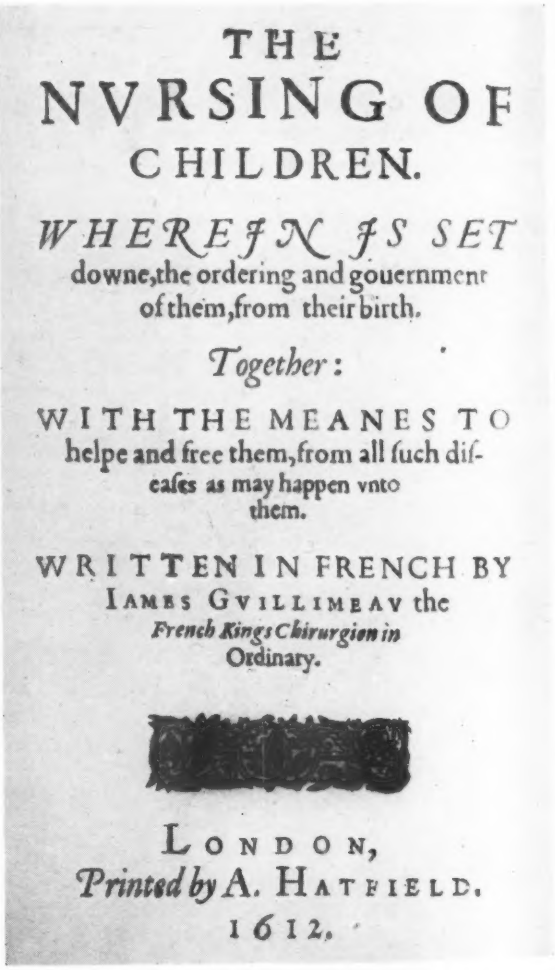
Jacques Guillemeau (born 1550), the French obstetrician, opens the seventeenth century with his work 'De la Nourriture et Gouvernement des Enfans' which was anonymously translated into English in 1612 under the title of 'The Nursing of Children'. This was bound with his treatise on midwifery and a copy of this edition, whose title page is reproduced here, is the oldest textbook in the library of St. Bartholomew's Hospital, London.

There is a well written preface eight pages long addressed to 'Ladies, wherein they are exhorted to nurse their own children themselves', in which he asserted that there was 'no difference between a woman who refuses to nurse her owne childe, and one that kills her child as soone as shee hath conceived', but without acknowledgement to Favorinus. He also related the classical story of the boy who in later years greeted his nurse with gold, but gave only silver to his mother because she had no alternative but to nourish him in her womb, whereas the nurse 'carried me three yeares in her armes, and nourished me with her owne bloude'.

Guillemeau enumerated his objections to wet nurses as follows: (1) The child might be changed and another put in his place. (2) the natural affection between mother and child declines. (3) Some bad condition or inclination may be derived from the nurse. (4) The nurse may impart some bodily imperfection, such as the 'French Pockes', to the child and thence even to the parents.

He believed that the qualities of temperament conveyed in the milk were more important than heredity, or, as he put it, 'Nurture prevails more than Nature'. Guillemeau concluded his preface with the oft-quoted story of Blanche of Castile, Queen of France, who, on learning that one of the ladies of the Court had just suckled her son, immediately thrust her finger down his throat to make him vomit the foreign milk which she believed would harm him.

Chapter I (pp. 1-8) deals with the 'nurse and what election and choice ought to be made of her'. He probably derived the major part from Paulus Aegineta, recommending that she should be of healthy lineage, good behaviour, sober, even-tempered, happy, chaste, wise, discreet, careful, observant, understanding, conscientious and always


THE
NVRSING OF
CHILDREN.

WHEREIN IS SET
downe, the ordering and gouernment
of them, from their birth.

Together:

WITH THE MEANES TO
helpe and free them, from all such dif-
eases as may happen vnto
them.

WRITTEN IN FRENCH BY
IAMES GVILLIMEAV the
French Kings Chirurgien in
Ordinary.

LONDON,
Printed by A. HATFIELD.
1612.

FIG. 5.—Title page of Jacques Guillemeau's work. Reproduced by kind permission of the Librarian, Medical College Library, St. Bartholomew's Hospital.

willing to give the breast. She should be physically healthy, with a pleasing countenance, 'ruddie mouth', and rosy complexion, and she should have 'veire white teeth' and broad but not pendulous breasts with good nipples; she should play with her charge and change him often. Guillemeau warned against redheads and his objection to them may either have been due to the fact that their fiery temperament would have been detrimental to the milk, or he may have shared the view of Mauriceau (1673) who objected to them because of their 'ill accents', and because their 'milke hath a soure, stinking and bad scent'!

Not only should the temperament, physique and complexion of the nurse be examined, but her milk also should be closely scrutinized. The milk should be sweet, odourless and white; blue milk indicates melancholy, yellow choler, and red means that it is not well concocted. If it is too watery scouring and undernourishment will follow, whereas if it is too thick the infant will be liable to indigestion, curdling, obstruction and stones. The nail test was modified to the extent of using a glass instead of the fingernail. Nurses were naturally prone to conceal the fact that their milk was failing for fear of losing their position, and to guard against deceit Guillemeau recommended frequent examination of the breasts to ensure continued activity and of the baby to see if he is 'bepissed'.

Chapter II deals with the nurses' 'dyet and manner of life', in which she is warned against bad air, bad smells, salty or spiced foods, garlic, mustard, stale cheese and also roast meat if the infant's complexion is moist or phlegmatic. She should spurn all raw fruit, and drink only ale, beer, barley water or wine, rest whenever she can, keep her bowels open and 'shun all disquietness of mind'.

The next three chapters deal with mothercraft and then on page 18 chapter VI he is concerned with the actual technique of feeding. The baby is kept away from the breast for at least eight days after delivery, and even as long as one month, i.e., until the mother is 'purified of her after-purging, as Hippocrates saith'. This is a longer period than Soranus advised, and he gives no instruction as to how the infant is to be nourished in the interim, but in order to establish and maintain lactation the mother is advised to allow 'little prettie whelps' or 'her keeper' to suck her breasts, or alternatively she should 'draw them with a glass'. When suckling eventually begins the infant is allowed to feed

> 'as often as he crieth' but 'only a little at a time, because the stomacke at first is but weake'. . . 'It is verie hard to set downe the quantitie of milke that a child should take; But therein the Nurse must have a respect to the age, complexion, temper, and to the desire which the child hath to sucke.'

In Chapter VII we find the earliest hint of the almost military form of discipline which subsequently steadily gained ground and reached a climax at the beginning of the present century. Guillemeau recommended that the infant be changed at 7 a.m., noon, 7 p.m. and midnight but, realizing that this was a counsel of perfection, he hastened to add that

> 'because there is no certain howre, either of the child's sucking, or sleeping: therefore divers, after he hath slept a good while do every time shift him; least he should foule and bepisse himself.'

Chapters IX and X deal with weaning which is begun when the upper and lower incisors have erupted with the giving of sops, bread, panada or gruel, and later (e.g. at about 15 months) minced poultry is added together with meat after the age of 2. Complete weaning was delayed until after all the teeth had erupted, and evidently quite a ceremony was customary. Spring or autumn were the seasons of choice and it was important to start during the waxing of the moon. Guillemeau describes a typical day in the weaning period as follows: (1) Change and breast feed on waking. (2) After an interval of two or three hours give panada, gruel, etc. (3) Two hours later give the second breast feed. (4) After another sleep, change him on waking, take him into the fresh air and then breast feed again. (5) After another sleep give dinner with boiled water to drink.

There is an interesting comment in the margin by the English translator who points out that the advice about boiled water refers only to France 'where they have not Ale or Beere'! If under the above regime the infant refuses to forsake the breast then the nipple should be anointed with aloes or mustard or the mother should be kept out of the infant's range of vision.

Caulfield (1932) has drawn attention to the hitherto unheeded work, the 'Countesse of Lincolnes Nurserie', which was written by Elizabeth Clinton, Dowager Countess of Lincoln, and printed in Oxford in 1662. It is short and is concerned with 'the duty of nursing, due by mothers to their own children'.

The worthy Countess had had 18 children of her own and all were 'reared' by wet nurses—that is to say most of them died in infancy. In fact only one son, Theophilus, reached majority to become the fourth Earl of Lincoln, and the book is dedicated to his wife, Bridget, who had the temerity to breast feed her first child and thereby put her mother-in-law to shame. It is greatly to the credit of the old Countess that she saw the error of her former ways

and decided to write this book by way of atonement. In it she cites Biblical examples of mothers who did their duty, e.g., Eve who fed Cain, Abel and Seth, and Sarah the wife of Abraham, whose example confirmed the Countess in her new belief that dry breasts constituted a confession of past wickedness, and that to withhold a full breast was to be 'more savage than dragons, and more cruel than ostriches to their little ones' (see Job, **39**, 16). She scornfully disposed of the fashionable objections to breast feeding, e.g., that it spoilt the figure, was 'noisome to one's cloathes', or interfered with gadding about, and she was in a strong position to describe the evils of wet nurses who were often slothful and deceitfully concealed their own failing supply of breast milk.

The Countess concluded her passionate appeal with the following exhortation:

> '. . . be not so unnatural as to thrust away your own children; be not so hardy as to venture a tender babe to a less tender breast; be not accessory to that disorder of causing a poorer woman to banish her own infant for the entertaining of a richer woman's child, as it were, bidding her to unlove her own to love yours.'

It is indeed remarkable that one of the nobility in the early seventeenth century should have felt strongly enough to have put pen to paper and so earnestly entreated those who came after her to avoid repeating her own mistakes.

Rickets in the Seventeenth Century

There can be no doubt that the disease known as rickets has occurred since the earliest historical times for, as we have seen, Soranus briefly described the characteristically crooked limbs, and skeletons have been found which provide material support for the contention. Hans Bergmaier's painting of the Virgin and Child, *c.* 1500 (see Drummond, *et al.*, p. 181) leaves no doubt that at that time the rachitic child was the accepted normal, but nevertheless there is compelling evidence to show that in the early seventeenth century there was a rapid rise in the incidence of florid rickets which assumed epidemic proportions, at any rate in the southern half of England. There has been a great deal of controversy about the origin of the word 'rickets' which has usually been regarded as a derivation from the Greek. Recently, however (Mitchell, 1951) it has been suggested that a 'Dr. Ricketts of Newberye' may have given his name to the disorder about 1620. The rise in incidence at about this time accounts for the fact that John Graunt, in the index to his 'Observations upon the Bills of Mortality' (1662), notes that 'the Rickets is a new disease, both as to name and to thing; that from fourteen dying thereof Anno 1634 it hath gradually encreased to above five hundred Anno 1660'. By careful reasoning Graunt calculated that this increase was real rather than apparent for the sum of all the likely causes of death, such as 'liver-grown', which might have masked the diagnosis of rickets in previous years, never amounted to anything like that figure.

It is not easy to account for the prevalence of rickets in the seventeenth century, but according to Drummond it was due to a fall in the calcium and phosphorus intake. Kellett (1934) states that in the days of Charles and Cromwell wheat prices were disproportionately high as compared with wages so that more than half the families were short of the bare necessities of life. The wool industry was at its height and children from the age of four upwards worked long hours at home quilling, spinning and weaving. Very cold winters (the Thames froze several times during this period) also probably aggravated the conditions. In later years, as we shall see, the Industrial Revolution resulted in a shift in incidence to the towns, but in Glisson's day rural communities seemed mainly to have been affected. It must not be concluded from this, however, that social conditions in the towns were satisfactory; in fact in London they have probably never been worse, culminating as they did in the Great Fire of 1666. Overcrowding was atrocious, and the general filth in the streets, in the homes and of the Londoners themselves was indescribable. Under such circumstances artificial feeding must have been extremely hazardous though no doubt it was occasionally successful.

Daniel Whistler (1619-84) wrote the first full clinical description of rickets in an M.D. thesis at Leyden in 1645 but the credit is usually given to Francis Glisson (1597-1677) who, independently wrote his famous treatise in 1650 entitled 'De Rachitide'. This work was translated into English in 1651 by Nicholas Culpeper (1616-54) himself the author of many medical books including an unoriginal work called 'A Directory for Midwives' which was bound with 'A Tractate of the Cure of Infants' (1675). Glisson's description is very full and at times most abstruse. In Chapter XV (pp. 155-163) he discusses predisposing factors in the parents such as their 'cold or moist distemper', or bleeding or suckling during pregnancy which 'defrauds the embryon of due aliment', and in the following chapter he deals with the causes incident to children after their birth, such as damp houses and overeating, especially highly spiced foods. Thus on page 169 he advises that:

> 'a plentiful Diet is altogether to be abandoned and a thin spare diet ought to be observed, for too liberal feeding doth overwhelm and choak the heat, and therefore must needs accumulate many crude and raw humors.'

He attributes the late manifestations of rickets to protection *in utero*, tight swaddling of the head and limbs during the neonatal period, and the wholesomeness of the diet in the first months:

> '. . . for Breast milk is the most solubrious and agreeable nourishment that tender age, especially when it is sucked from the breasts; for it is a simple and uniform meat, full of nourishment, easie to concoct, and friendly and familiar to the constitution of Infants.'

After the age of 9 months children are fed with other aliments besides breast milk, and the resulting dietary errors were largely responsible for the development of rickets, which, according to Glisson, was not a contagious disease.

Although there has been considerable controversy amongst the experts (see Still's 'History of Paediatrics', p. 221) concerning Glisson's claim to priority with regard to his description of rickets, there can be no question that his brief comments on scurvy (p. 249), which is 'sometimes conjoyned with this Affect', is the earliest record of this disease in infancy. When rickets was complicated by scurvy the infant showed intolerance to purgation, was 'much offended by violent exercise', and suffered from 'divers pains running through the Joynts'; tumours of the gums were also often present. This remarkable piece of clinical observation and diagnostic differentiation has not received the merit it deserves.

Robert Pemell (?-1653) was a general practitioner in the, at that time, flourishing town of Cranbrook in Kent. In 1653 he wrote the second English paediatric textbook on the lines of Phayer's work as opposed to those written by the pens of obstetricians (e.g. Roësslin and Guillemeau) to which a section on the care and management of infants was appended. Pemell was primarily concerned with children's diseases rather than with infant feeding but nevertheless he attributed the majority of symptoms to errors of diet. For example, in chapter 4 on page 6 he wrote:

> 'The falling sicknesse cometh sometimes by consent of the inferior or lower parts especially of the stomach and bowels, when milk is corrupted in the stomach, or hath an ill quality, which doth often happen when the nurse is of an ill complexion, or from the nurses ill dyet, and to frequent drinking of wine, and so ill vapours arise from the stomach too the brain. . .'

and again in chapter 10 on page 20:

> 'The cause of watchings is the corruption of the milk, or too much milk, which putrifieth in the stomach, from whence sharp vapours arise continually to the brain. . .'

In addition stomatitis, worms, cough, rheume, shortness of breath, the hicket, gripings and frettings of the belly and looseness and flux of the belly are all due to 'corruption of the milk', or 'abundance of milk oppressing the stomach'. On the other hand if vomiting was due to an abundance of milk it was not considered to be dangerous but was rather looked upon as a good sign indicative of a strong and healthy baby. The remedy in this case was simple: 'Let not the child suck so often, nor so long'.

Walter Harris (1647-1732) was a physician who could most certainly claim to be both original and remarkably influential, but this was all the more unfortunate because he was so misguided. His 'De Morbis Acutis Infantum' (1689) was translated into English by William Cockburn in 1693, and it passed through 18 editions as well as being translated into various foreign languages. It was included in the anonymous compilation entitled 'A Full View of all the Diseases Incident to Children' in 1742.

The secret of his success lay in the simplicity of his hypothesis that 'all the complaints of Infants spring from an Acid as their Common Source', and this original point of view was particularly appealing at a time when the old humoral pathology was beginning to fall into disrepute. In this way it was easy to account for the curdled milk, sour breath, acrid-smelling stools and excoriated buttocks, to say nothing of diarrhoea and vomiting, asthma and the King's Evil, for all of which the universal remedy was the free use of testaceous powders made from oyster shells, crab's eyes and claws, etc. The therapeutics of infancy were to be confined by this theory for more than a century, and even today the conception of 'acidity' is prevalent amongst the laity.

Harris was rightly most concerned about the fashionable practice of both high and low ladies of farming out their babies to irresponsible women in the country who soon neglected their charges. This is well illustrated by the passage in which the Rector of Hayes in Kent told Harris that

> 'his parish . . . was, when he first came to it, filled with suckling infants from London, and yet, in the space of one year, he buried them all except two; and that the same number of small infants being soon twice supplied, according to the usual custom with hireling nurses, from the very great and almost inexhaustible city he had committed them all to their parent earth in the very same year.'

According to Harris the maladies of infancy could be immediately attributable to their catching cold,

the too thick milk of the nurse, their over-soon eating fleshes, and the mad and imprudent fondness of mothers and many nurses who often permit them to 'sip up wine and other strong and spirituous liquors, which are very heating'. Thick milk, which resulted from the nurse indulging in venery and drunkenness, tends to clog the infants' 'conduits for transmitting of chyle', and flesh meat produces sequelae which are 'almost inseparable from the overfeeding of tender infants'.

The giving of wines and spirits, and opiates in the form of Godfrey's cordial or Dalby's carminative, to young infants was a common and pernicious habit amongst the nurses of that time and was responsible for many infant deaths:

> 'There are some wicked Nurses, reckoned more skillful than the rest, who commonly attend lying-in women during the Month, and are not afraid to give Wine and Brandy, sweetened perhaps with Sugar, to new-born Infants with great Secrecy, as often as they can conveniently to still their crying, and procure Ease to themselves; whence dreadful Symptoms arise from hidden Causes. The same Crime is frequently committed by Nurses that suckle at their own Homes, who not only themselves guzzle down a great Quantity of strong Beer and burning Spirits, and thereby heat and spoil their own milk, but also boldly give the same to the tender infants committed to their care, and especially in those Gripes which they have occasioned by their improper Diet or Intemperence.'

The results of the gross mismanagement by the nurses were plain for all to see; compare, he says, 'the healthy sturdy race of children brought up in the cottages upon the plainest Victuals, with the tender valetudinerary Offspring of Great men, wallowing in luxury from the very cradle'.

Walter Harris was not a likeable man for his book is full of false modesty, but he clearly perceived the dangers and evils of the fashionable methods of rearing infants in his day, and he was not afraid to attack them in public.

John Pechey (1655-1716) is best known as the translator of Sydenham's works, but he also compiled a 'General Treatise of the Diseases of Infants and Children' from several authors in 1697, and he is therefore a fitting writer with whom to round off the seventeenth century. He was very human in his approach to the subject, and he followed up a list of the usual characteristics desirable in a good wet nurse with the addition that she must be 'merry and cheerful, and smile often to divert the child'. On page 5 he remarked that 'if watchings are troublesome, sleep must be endeavoured by Singing, Rocking and offering the Teat often', but he was careful to add that 'the Stomach must not be overburthened with milk', for 'Iniquity is connatural to Infants, and they are more prone to Evil than to Good, we must not therefore indulge them too much'. Milk was recommended as the only food for infants for some months and then pap might be given but no solid food was to be offered before the teeth had erupted, and it should then be introduced gradually, the nurse first chewing it in her own mouth. Overfeeding, or sucking too greedily, results in frights in the sleep, looseness and vomiting, but the latter may also be due to corruption of the milk, worms, weakness of the stomach (pyloric stenosis?) or 'Nurses eating windy things'.

In concluding the seventeenth century writings on infant feeding it is encouraging to be able to record Pechey's remark in the preface of his compilation that 'Children, if they are virtuous, are great Blessings, and a publick good'.

Influence of Social Factors on Infancy in the Eighteenth Century

Infant life during, and for long before, the eighteenth century was valued by the majority of the populace no higher, and probably somewhat lower, than that of the average pet dog or cat today, in spite of Pechey's humanitarian outlook. But towards the latter half of the century definite signs of an awakening of the public conscience appeared, together with a growing interest in infant care and management and an expanding knowledge of children's diseases. Previously therapeutics had been dominated by witchcraft and the ancient humoral pathology, but, as we have seen, Walter Harris threw fresh light on the scene which, in spite of being misleading, was also stimulating. From the humanitarian aspect, in England the perseverance of two great eighteenth century philanthropists, Thomas Coram and Jonas Hanway, was largely responsible for the initiation of the outstanding improvement in the social status of infancy.

Thomas Coram (1668-1751) retired to live in Rotherhithe after spending many years at sea engaged as a shipmaster between England and her colonies which afforded him ample opportunities for performing good deeds towards slaves and other needy persons with whom he came in frequent contact. In London he was at once disturbed by the sight of dying children in the streets, and by the bodies of dead infants rotting on the dung heaps. Spurred on by this for the next 17 years, but handicapped by the lack of financial support and by the apathy and prejudice of all around him, he toiled to set up a hospital for foundlings. Success finally crowned his efforts when one was eventually opened in Lamb's Conduit Fields in 1741.

From the moment of the inception of the

Foundling Hospital it was clear that a most urgent need had been fulfilled, and by 1753 no less than 116 infants were offered for admission on a single day. Because of this overwhelming popularity the Governors decided to appeal to Parliament for funds, and in 1756 these were granted with the proviso that the charity be extended to all exposed and deserted children. In the course of the next five years, £50,000 was spent and the Hospital became a dumping ground for all unwanted infants who were sent to London from all over the country. Transport was a difficult problem and a terrible system rapidly developed whereby unscrupulous escorts were engaged to convoy the infants for a relatively small fee. The escorts usually spent the money on alcohol en route and the infants were so neglected that they frequently died before reaching London or were delivered on the doorstep in a moribund state. Of 15,000 infants admitted to the Hospital during this time, 10,000 died but this great wastage of human life was calmly attributed by many worthy citizens to 'the profuse waste and imperfect workmanship of nature', and in any case it was regarded as a suitable fate for the offspring of harlots since it prevented them from perpetuating the sins of their mothers. The nobility often found abandoned infants 'drop't' on their doorsteps but they seldom took pity on them for fear of encouraging vice or establishing a precedent, and they would rather send them to the care of the parish although this was known to mean an almost certain death sentence.

Parliament subsequently withdrew its support to the Hospital and for a while the Governors demanded a fee of £100 for each infant admitted, but later this was dropped and admissions were confined solely to illegitimate infants born to previously righteous women. Nevertheless this charity, for all the good that was done, was given a mixed reception, for example, in the satirical poem entitled *Scandalizade* by 'Porcupinious Pelagius' addressed to Coram in 1750 (quoted by Betsy Rodgers, 1949):

> 'The Hospital Foundling came out of thy Brains,
> To encourage the progress of vulgar Amours,
> The breeding of Rogues and th'increasing of Whores,
> While the children of honest good Husbands and Wives
> Stand exposed to Oppression and Want all their Lives.'

Nevertheless Hogarth was proud to paint Coram and Handel gave an organ to the Hospital in appreciation of the good work that was being done (Trevelyan, 1944).

Jonas Hanway (1712-86) was particularly interested in the fate of infants left to the care of the parish, and he made an extensive tour of England ('A Journal of Eight Days Journey', 1757) to study this pressing problem. It was the duty of the parish overseers to track down the father of an illegitimate child and extract a fine of £10 from him, ostensibly to be used to cover the expenses involved in the care of the mother and baby, but in fact pocketed by them except for the small fee which was payable to the unscrupulous nurse to whom the infant was farmed out. The parishes kept records of women willing to take these infants, and Hanway found in them references to 'excellent killing nurses'. In his 'Plea for Mercy to the Children of the Poor' he estimated that only one in 70 entrusted to the parish survived to grow up, thence to be sent out into the streets to beg (maimed if necessary), steal or become prostitutes. The average workhouse was described by Hanway as being dirty, old and crowded with sickly, aged and filthy people, and he added 'how could it be conceived that the infant could open its mouth without sucking in mortality? How many of the poor babes had gin and sleeping potions given them by their nurses I know not' (quoted by Rodgers, 1949). As a first step towards remedying this disgraceful state of affairs he forced a bill through Parliament making compulsory the registration of all poor infants under the age of 4, and this in itself produced fresh evidence of the appalling conditions prevailing at the time. In the parish of St. Clement Danes for instance (Caulfield, 1931), of 23 children committed to the care of one Mary Poole at two shillings a week, 18 died within the year. A second Bill in 1767 provided for the dissemination of all children under the age of 6 from the workhouses to registered foster parents, who were to be paid two shillings and sixpence weekly, with a reward of ten shillings if a child under the age of 9 months lived for one year, and a bonus of five shillings if it recovered from measles or whooping cough. If two children died under the care of the same nurse within a year she was to be disqualified from taking further charges.

The bills of mortality, the only yardstick with which we can measure the degree of improvement resultant upon all this activity in the social sphere to improve the lot of infants, were unfortunately grossly inaccurate, depending as they did upon the number of christenings rather than births, and upon the number of burials of those belonging to the Established Church rather than the total deaths. Furthermore the cause of death was defined and recorded by the searchers, a squad of unscrupulous women who were only too ready to accept bribes to conceal the true circumstances of the death. The deaths of infants were all lumped together under the

age of 2, which corresponded with the teething period, and also conveniently with the most popular diagnosis of the searchers. Edmonds (quoted by Caulfield, 1931), an early Victorian statistician, computed that between the years 1730 and 1749 60·2% of all infants died under the age of 2 (probably 75% died under the age of 4 in London alone at this time), whereas by 1790 to 1810 the figure had undergone the remarkable reduction to 30·3% mortality before the second birthday.

The mortality in the foundling hospitals also experienced a welcome decline. Thus the London Foundling Hospital, which originally showed a mortality of about 66·6%, had reduced this to about 52% by 1760 and to 17% by 1860. The Paris foundling hospital, which was founded as early as 1670, had a mortality of about 80% in the first year of life in 1770 (when the rate of admissions was over 5,000 yearly) but by 1820 this was reduced to approximately 50% in the first year and 74% under the age of 5. This prompted the cynical suggestion that the inscription over the door should read 'Ici on fait mourir les enfans'.

It is essential to take into account the social conditions of the times when considering the history of infant feeding, for they have a profound bearing upon the whole problem. Many infants fared badly and died simply because their lives were valued so cheaply that in many instances no food at all was given, the unwanted infant thus swelling the ranks of stillbirths, the overlayed, and those dying from 'want of breast milk'. Those who survived often did so on a diet which Sir William Fordyce so well described in 1773:

> '. . . they are fed on meat before they have got their teeth, and what is, if possible, still worse, on biscuits not fermented, or buttered rolls, or tough muffins floated in oiled butter, or calves-feet jellies or strong broths yet more calculated to load all their powers of digestion.'

(From 'A New Enquiry into the Causes, Symptoms and Cure of Putrid and Inflammatory Fevers' by Fordyce, quoted by Drummond, 1940.)

Accurate statistics would be required to assess the relative importance of bad social conditions and bad feeding methods in causing the astonishingly high infant morbidity and mortality, but obviously they will never be available for this period. We can learn a good deal, however, from Sir Hans Sloane's letter to the Vice-President of the Foundling Hospital in which he wrote that the mortality of hand-fed infants was 53·9% as compared with 19·2% for those suckled at the breast. The French figures by M. Villesmé (quoted by Charles West, 1852) are also very instructive since they refer to the mortality of *enfans trouvés* treated at three separate foundling hospitals with differing feeding regimes: At Lyons foundlings were boarded out to wet nurses within one week of reception; the mortality in the first year of life was 33·7%. In Paris foundlings were suckled by wet nurses in the hospice; the mortality was 50·3%. At Rheims foundlings were boarded out early but were mainly hand reared: the mortality was 63·9%.

There are no comparable mortality figures for normal babies born in wedlock apart from contemporary statistics from the lying-in hospitals (Underwood, 1819). In the British Lying-in Hospital, where mothers and babies stayed for three to four weeks, between the years 1783 and 1791 112 out of 5,233 infants died, i.e., a neonatal mortality of just over 2%. In Dublin, where they stayed for only two weeks as a rule, the mortality for that period was about 4%. These figures, if reliable, are remarkably good and they are very probably dependent upon the high incidence of breast feeding, without the addition of other foods, in these early weeks. For older infants the differentiation between hand and breast feeding became progressively meaningless in the eighteenth century since it was probably universally customary to give pap and panada in addition to the breast. De Claubry in 1783 (quoted by Drake, 1931) described pap as 'the most dangerous of all foods for infants' in that 'it has caused to perish a great number, or has rendered them infirm and diseased all their lives'. The terms pap and panada were sometimes used synonymously but more often the latter referred to cereals cooked in broth. Great quantities were often stuffed down the infants' throats having been previously chewed by the nurse to facilitate digestion, who then gave them the breast 'to better dilute the pap' (Ettmuller, 1703). Drake shows a picture of a metal pap spoon dated about 1800 with a narrow slit at one end which was cleansed by inserting a blade of a knife, and a hollow handle at the other end down which the nurse blew to hasten the delivery of the pap.

We may therefore conclude that the social conditions prevailing at the time and the popular methods of infant feeding were both responsible for the high rate of infant mortality in the eighteenth century. Even when the social circumstances were first class, bad feeding methods would take their toll, witness the experience of the Countess of Lincoln at the end of the sixteenth century and of Queen Anne (all of whose 18 children died in infancy) at the beginning of the eighteenth century; conversely, in the most humble of homes no doubt many poor mothers successfully reared their offspring on the breast. Between these two extremes

all grades of relative importance between these two major factors determining the infant mortality rate would be found.

The Employment of Wet Nurses

The eighteenth century is a convenient stage to refer in more detail to the employment of wet nurses for it was during this period that they enjoyed peak popularity in England amongst the aristocracy. Towards the end of the century we find evidence of their declining popularity in the writings of George Armstrong (1783) who definitely preferred dry- to wet-nursing, but it is important to remember that Armstrong worked mainly amongst the poor who were unable to afford the luxury of a wet nurse. The majority of eighteenth century writers, e.g. Richard Conyers (1729), deplored the use of pap for the newborn and preferred wet nursing to hand rearing mainly on the grounds that cow's milk promotes acidity. The fact that relatively few families could afford them did not concern those doctors whose patients were largely recruited from the upper social classes.

We have already seen that in Biblical times wet nurses were well organized on a financial basis, and since the time of Soranus the desirable characteristics of a good wet nurse have been slavishly copied from book to book up to 100 years ago when they were still to be found in Charles West's lectures to the students. Perhaps, however, they have never been more pleasingly recounted than by S. de Saint-Marthe who wrote the 'Paedotrophia' in Latin in 1584, which was subsequently translated into English by H. W. Tytler in 1797:

> 'Chuse one of middle age, nor old nor young,
> Nor plump nor slim her make, but firm and strong,
> Upon her cheek, let health refulgent glow
> In vivid colours, that good-humour shew;
> Long be her arms, and broad her ample chest;
> Her neck be finely turn'd, and full her breast:
> Let the twin hills be white as mountain snow,
> Their swelling veins with circling juices flow;
> Each in a well projecting nipple end,
> And milk, in copious streams, from these descend;
> This the delighted babe will instant chuse,
> And he best knows what quantity to use.
> Remember too, the whitest milk you meet,
> Of grateful flavour, pleasing taste, and sweet,
> Is always best; and if it strongly scent
> The air, some latent ill the vessels vent.
> Avoid what, on your nail, too ropy proves,
> Adheres too fast, or thence too swiftly moves.'

The nail test has survived, unchanged, for over 1,200 years! The above quotation is taken from the second book of Tytler's original translation, and it is interesting to compare this with the version on page 234 of Struve's 'Treatise' (1801) in which the two lines bracketed above were omitted. Like many historical and contemporary writers on infant feeding, Struve evidently had no confidence in the infant's ability to regulate the intake of milk in accordance with his requirements.

Didactic poems, which were popular at this time (e.g. Downman, 1788), usually preceded a description of the perfect wet nurse by a vehement exhortation to mothers to feed their own children, and Claude Quillet's 'Callipaedia', written in Latin in 1655 and translated into English in 1712, by Nicholas Rowe, the Poet Laureate, was no exception. The following extract is taken from Book IV, page 16:

> 'Say, therefore are not those absurdly vain,
> Who cause their Children's fate and then complain;
> Who with a hopeful beauteous Offspring blest
> Forget themselves, and hire unwholsom Breasts;
> And to some common Wretch commit the Care,
> Of infant Celia or the future Heir:
> Besides Diseases and unnumbered Ills
> That latent spread and flow in Milky Rills
> That from bad Teats and putrid Channels pass
> And taint the Blood and mingle with the Mass,
> The noxious Food conveyes a greater Curse
> And gives the meaner Passions of the Nurse.
> Th'unthinking Babe sucks in the deadly Bane
> And new-form'd Lusts the native Virtue stain;
> Who draws the flaggy Breasts of Wanton Dames
> Shall base Desires imbibe, and burn with guilty Flames.'

In the seventeenth and eighteenth centuries the ladies of quality did not breast feed their own infants because it was unfashionable, because they feared it might injure their health and ruin their figures, and above all because it would interfere with the social round of returning 'favours', playing cards and visiting the theatre. Neither lyrical appeals such as appeared in the 'Callipaedia', nor 'pious perswasives' such as Henry Newcome's 'The Compleat Mother' (1695) in which 46 of the total 112 pages are filled with Biblical quotations supporting his theme, were able to make much impression upon the dictates of fashion and the caprices of the aristocracy. Fathers encouraged this behaviour and on the pretext of sending them out of town into the country air, the infants were farmed out to nurses with the disastrous results recorded by Harris. Some fathers employed nurses with the deliberate intention of doing away with the infant and one, in 1740, angered by the cries of a new addition to the family, threatened to 'hire a nurse to overlay him'.

Wet nurses were often employed in the home, and on the birth of the Prince of Wales (later George IV) in 1762 it was officially announced: 'Wet-nurse, Mrs. Scott, Dry nurse, Mrs. Chapman, Rockers, Jane Simpson and Catherine Johnson' (Caulfield, 1931). Indeed the lot of wet nurses

became so enviable that many poor young girls contrived to become pregnant, and then overlayed or 'drop't' the infant before seeking employment. Doctors and accoucheurs kept a 'nurse-book' and the standard rate of pay was ten to twelve shillings weekly with all found. Thus the high rate of infant mortality was in part the source, and in part the effect, of the ample supply of wet nurses. This sad state of affairs stimulated Archbishop Tillotson, Addison, Swift and many others to exhort ladies of fashion to breast feed for the mutual benefit of mother and child.

In France, characteristically, wet nurses were highly organized from the twelfth century onwards (Drake, 1935) and by 1715 four employment bureaux existed in Paris for the registration of nurses who were required to give their name, age and details of the age and condition of their own baby. *Recommandaresses* were in charge, and for a time there were many abuses, but a new law in 1762 forbade nurses from taking charge of an infant unless her own was older than 9 months. The new legislation also provided for regular medical inspection of the nurses, and the compulsory provision of a separate cradle to prevent overlaying the nursling. Fees were fixed by law and the nurses were protected by the threat of imprisonment for those who failed to pay them (though this was repealed after the Revolution in 1792).

It seems not unlikely that had such a realistic approach to the problem been adopted in England, the lot of the average infant in the eighteenth century would have been considerably improved. The whole problem of the official recognition of wet nurses in France and in England has a close parallel in the different methods of treatment of prostitutes in the two countries. Whereas in France both problems have been recognized and at least partly solved, in Britain, and particularly in Scotland, there has always been a tendency to pretend that they do not exist.

(*References will be appended to Part V.*)

PROFESSOR LUIGI SPOLVERINI

Professor Luigi Spolverini, President of the Italian Society of Paediatrics, will be 80 years old on August 29, 1953. His many contributions to paediatric literature—some 150 in number, spread over 53 years—have covered a wide range of subjects and have brought him renown far beyond the boundaries of his own land. His interests have ranged from the composition of breast milk to thyroid dysfunction, from rheumatic heart disease to the reduction of infant mortality. He is perhaps most widely known for his part in the organization of the campaign against poliomyelitis. Many countries have honoured him, and in 1934 he was elected an honorary member of the Section of Paediatrics of the Royal Society of Medicine.

The Editors of the *Archives of Disease in Childhood* are sure that its readers will join them in offering Professor Spolverini their best wishes on his eightieth birthday.

BRITISH PAEDIATRIC ASSOCIATION

PROCEEDINGS OF THE TWENTY-FOURTH GENERAL MEETING

The twenty-fourth annual general meeting of the British Paediatric Association was held at Windermere from April 23 to 25, 1953.

BUSINESS PROCEEDINGS. The President, Professor J. M. Smellie, was in the Chair and the following members were present:

F. M. B. Allen, E. C. Allibone, I. Anderson, J. Apley, Cecile Asher, H. S. Baar, M. Bodian, R. E. Bonham Carter, Frances Braid, J. V. Braithwaite, P. Bray, R. W. Brookfield, D. Browne, W. A. B. Campbell, N. B. Capon, W. H. P. Cant, I. A. B. Cathie, N. Clark, T. Colver, Beryl Corner, D. Court, J. Craig, W. S. Craig, Mildred Creak, J. Crooks, V. Mary Crosse, G. Davison, R. H. Dobbs, E. Dott, J. L. Emery, F. J. Ford, Isabella Forshall, A. W. Franklin, D. Gairdner, W. Gaisford, R. R. Gordon, S. Graham. C. F. Harris, J. D. Hay, P. Henderson, J. L. Henderson, A. Holzel, D. V. Hubble, J. H. Hutchison, R. S. Illingworth, Ursula James, H. E. Jones, F. F. Kane, J. Kempton, R. Lightwood, P. MacArthur, Agnes MacGregor, M. MacGregor, Helen Mackay, R. MacKeith, F. J. W. Miller, R. A. Miller, A. Moncrieff, G. H. Neligan, G. H. Newns, D. N. Nicholson, A. P. Norman, A. G. Ogilvie, J. N. O'Reilly, W. W. Payne, C. P. Pinckney, C. T. Potter, B. Schlesinger, W. Sheldon, Victoria Smallpeice, J. M. Smellie, J. F. Smith, R. E. Smith, J. Spence, R. E. Steen, K. H. Tallerman, M. L. Thomson, J. P. M. Tizard, R. McL. Todd, C. W. Vining, H. K. Waller, A. Watkins, H. P. Williams, T. P. Williams, Mary Wilmers, D. W. Winnicott, Winifred Young, S. Yudkin, R. B. Zachary.

The Association had the honour of entertaining Mr. A. Gemmell, President of the Royal College of Obstetricians and Gynaecologists, at the annual dinner, and there were 33 guests present at the meeting together with Professor A. C. Frazer, who gave the Windermere Lecture.

The minutes of the last annual general meeting were approved.

ELECTION OF OFFICERS. The following were elected by ballot for the year 1953-54:

PRESIDENT: Dr. B. E. Schlesinger.
TREASURER: Dr. R. C. Lightwood.
SECRETARY: Professor A. Moncrieff.
EXECUTIVE COMMITTEE (for three years):
Dr. J. Forest Smith.
Dr. G. H. Newns.
to replace Dr. C. T. Potter and Dr. B. E. Schlesinger.

ELECTION OF NEW MEMBERS. The following were elected by ballot to membership of the Association:

HONORARY MEMBERS:
Mr. R. Coyte
Professor J. M. Smellie

CORRESPONDING MEMBERS:
Professor G. Frontali (Rome)
Dr. I. McQuarrie (Minneapolis)
Dr. T. McNair Scott (Philadelphia)
Dr. Jessie Boyd Scriver (Montreal)
Professor A. Sundal (Bergen)

ORDINARY MEMBERS:
Dr. P. Bray (Cardiff)
Dr. D. M. Douglas (Edinburgh)
Dr. Ursula James (London)
Dr. J. J. Kempton (Reading)
Dr. M. MacGregor (Warwick)
Dr. G. A. Neligan (Newcastle)
Dr. J. P. M. Tizard (London)

The TREASURER'S REPORT was received and approved.

The REPORT OF THE EXECUTIVE COMMITTEE was received and approved and is printed below.

The Hon. Secretary made a statement on the forthcoming International Paediatric Congress.

Professor W. Gaisford made a statement on the proposed inquiry into paediatric education.

NEXT MEETING. It was agreed to accept the recommendation of the Executive Committee that Windermere should be regarded as the regular meeting place.

COMMITTEE ON ADOPTION. Members were invited to send in any comments on adoption which they wished brought before the Committee on Adoption now sitting at the Home Office.

The presidential badge of office and the candelabra purchased in memory of the late Sir Leonard Parsons were used for the first time at this meeting. Dr. B. Schlesinger presented to the Association an illustrated book on the work of Louis Oscar Roty, the artist responsible for the medallion from which the presidential badge was made.

Report of the Executive Committee 1952-53

1. The Association will wish to congratulate Professor R. A. McCance and Professor A. Moncrieff on the award of the C.B.E., Dr. C. F. Harris on election as Dean of the Faculty of Medicine in the University of London, Professor C. McNeil on his nomination for Hon. LL.D., Edin-

burgh, and Dr. W. Sheldon on his appointment as Physician-Paediatrician to H.M. the Queen.

2. The Executive Committee has met three times since the last Annual General Meeting and the following is a summary of matters with which it has been concerned.

3. LEONARD PARSONS MEMORIAL AND PRESIDENTIAL BADGE. A sum of £136 was collected to provide a memorial to Leonard Parsons. It has been decided to expend a portion of this on a pair of Sheffield plate candelabra, suitably engraved, which will decorate the top table at the Annual Dinner. It was also decided to purchase an antique medallion showing a mother and child, and to have this mounted to make a presidential badge of office. This would also be paid for out of the memorial fund. The Association is indebted to Dr. B. E. Schlesinger for his efforts in finding suitable articles in each case.

4. INTERNATIONAL PAEDIATRIC CONGRESS. Members have been circulated with the preliminary programme of the proposed congress in Havana. It is hoped that some delegates will be able to go from the United Kingdom.

5. ARCHIVES OF DISEASE IN CHILDHOOD. It was decided to appoint Dr. J. D. Hay and Professor A. V. Neale to the Editorial Committee for 1954 in place of Professor R. S. Illingworth and Professor J. M. Smellie.

6. MEETING WITH FRENCH PAEDIATRICIANS. Twenty delegates from the Association and the Paediatric Section of the Royal Society of Medicine visited Paris in June, 1952, for a successful joint meeting with French colleagues. A visit of French paediatricians to London, has been arranged for May 7 to 10, 1953, with the Association and the Paediatric Section of the R.S.M. as joint hosts.

7. PRE-REGISTRATION POSTS IN PAEDIATRICS. It has been agreed to postpone discussion on this subject for the present except to suggest that the first six months after qualification is not a suitable period for a paediatric resident appointment.

8. FUTURE OF CHILDREN'S HOSPITALS. A memorandum on this subject received from members in Sheffield was forwarded to the Royal College of Physicians where the Paediatric Committee has begun consideration of this subject. A sub-committee of the Association has been set up to prepare evidence to submit to the College Committee.

9. REGIONAL PAEDIATRIC SOCIETIES. Careful consideration has been given to the question of meetings of the Association other than the annual meeting and it has been decided that for the time being it is better to foster the development of regional societies. A list of these was published in the February issue of the *Archives of Disease in Childhood.*

10. ANNUAL MEETING ARRANGEMENTS. The Executive Committee will suggest at the Annual Meeting that Windermere should be regarded as the regular meeting place. Further consideration is to be given to the whole policy of the choice and number of guests.

11. VISIT TO HOLLAND, 1954. A cordial invitation has been received from the Dutch Paediatric Society for a visit of 25 members to Holland in May, 1954. Further details will be circulated in due course.

12. PAEDIATRIC EDUCATION. The Association is collaborating in a survey of paediatric education in Europe organized by the International Paediatric Association and the World Health Organization. Professor W. Gaisford has undertaken to collect information and he visited Zurich in March to discuss details.

13. WORK OF SUB-COMMITTEES. The most important work during the year was the preparation by the tuberculosis sub-committee of a revised version of the pamphlet on the prevention of tuberculosis in childhood issued by the Joint Tuberculosis Council. The nursing joint sub-committee has learnt with interest that their nurse colleagues have changed their name to 'The Association of British Paediatric Nurses'. A special sub-committee was set up to answer certain questions for the Ministry of Health on the future arrangements for the supply of vitamin C.

14. ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS. Agreement has been expressed with a resolution of the Council of this College regarding the responsibility of the obstetric house surgeon for the care of the newborn baby to the paediatrician or his deputy.

15. The Association has suffered the loss since the last Annual Meeting of Hugh Ashby and Catherine Chisholm.

Scientific Communications

Professor A. C. Frazer delivered the George Frederic Still Memorial Lecture for 1953 entitled 'Absorption from the Intestines'.

DR. R. H. DOBBS (London). 'Treatment of Gastro-enteritis with Antibiotics.' The results of the Medical Research Council's trials on antibiotics in the treatment of gastro-enteritis were presented. These indicated that chloramphenicol and sulphadiazine were effective in significantly reducing the duration of the disease, and that over 90% of both mild and severe cases made straightforward progress compared to control groups in which progress was

delayed in one-third of mild and two-thirds of severe cases.

Aureomycin appeared to be a less effective drug, but there was evidence that this may have been more apparent than real.

In the discussion evidence was presented which suggested that these drugs varied in their effectiveness from time to time, and this variability was associated with the sensitivity of organisms of the *Bact. coli* group isolated from stool culture.

DR. O. P. GRAY (Cardiff), introduced by Professor A. G. Watkins. 'Hydatid Disease in Childhood.' The cases of hydatid disease seen in Cardiff were reviewed.

The cysts occur commonly in the liver and slightly less frequently in the lungs. Cysts have also been encountered in the brain and mesentery. All the children in the series with hepatic cysts had enlargement of the liver. Symptomless abdominal enlargement caused by the hepatomegaly was the usual presentation. Lower chest pains occurred with an infected cyst. Surgical treatment of the cysts is advocated.

Pulmonary hydatid cysts are usually diagnosed by radiography. Simple cysts appear as rounded opacities. Rupture of a cyst leads to characteristic radiographic appearances. Partial rupture is associated with a small crescent of air around the cyst, termed the perivesicular pneumocyst. With partial rupture of a cyst the membranes rest on top of the fluid, giving the appearance of the 'water lily' cyst. Pulmonary hydatid cysts are dealt with very satisfactorily by operation.

Intracranial hydatid cysts are situated in the cortex. They cause convulsions and hemiparesis with the signs of a space-occupying lesion.

The Casoni reaction is useful in diagnosis if care is taken to use fluid of known standard antigenic potency.

The Welsh sheep are more infected with hydatid cysts than sheep in other parts of Great Britain. The crowded mining villages are very close to grazing land; moreover, the sheep form part of the communal life of the village. This partially accounts for the fact that hydatid disease is endemic in Wales.

DR. J. P. M. TIZARD (London). 'Sensory Defects in Infantile Hemiplegia'. Dr. Bronson Crothers and the author recently re-examined 52 patients of varying age and intelligence with infantile hemiplegia. About two out of three had severe sensory defects. Methods of testing sensation in children were described. A film was shown comparing the mapping of visual fields by confrontation methods with unilateral and bilateral stimuli. Out of 38 patients who could be tested adequately, 19 had field defects, mostly homonymous hemianopia. Twenty-two out of 34 patients had defects of cortical sensory modalities (position sense, two-point discrimination, stereognosis) in the affected limbs and about half of these had also some loss of appreciation of light touch, etc. Of 41 patients whose limbs were measured, sensory abnormalities were found in all 29 who had undergrowth on the affected side. Nearly all had peripheral cortical sensory loss and more than half had visual field defects. Some of the 12 without shortening of the limbs had severe motor defects, but apart from one with hemianopia, no sensory abnormalities.

Hemianopia appears to cause little disability, possibly due to frequent, rapid, involuntary, lateral movements of the eyes towards the blind side. Loss of position sense in the affected arm seemed, as might be expected, to make attempts at 'muscle training' useless.

DR. J. G. MILLICHAP (London). 'Nephrotoxic Effects and Other Attributes of Drugs Used in the Treatment of Petit Mal.' Of 20 children with minor epilepsy who were treated with a new compound, 'milontin', 10 showed microscopic urinary abnormalities.

A similar nephrotoxic effect, hitherto unreported, was also observed in children given moderate doses of 'tridione' and 'malidone'.

Since leucopenia, a side-effect common to both these drugs, has not yet been reported with 'milontin', its clinical trial was continued. Its efficacy, at least equal to that of other agents, was significantly related to the type of minor seizure. Pure petit mal was controlled four times more effectively than the akinetic form. The latter, in the majority of patients, was combined with grand mal, and better response was obtained with the anticonvulsant, 'mysoline'.

Rather than a variety of petit mal, an akinetic attack should be regarded as a minor manifestation of major epilepsy, in which milontin and other related drugs are contraindicated.

The mode of action of milontin on the diencephalon, the site of origin of the petit mal discharge, was studied in rabbits by the use of radioactive isotopes. Its effect on the brain capillaries was similar to that observed on the renal glomeruli. The permeability was increased in both.

DR. J. H. HUTCHISON (Glasgow). 'Radio-Active Iodine Studies in Goitrous Cretinism.' The results of radio-active iodine studies in 12 cases of non-endemic goitrous cretinism were described. The ages of the patients ranged from 2 to 20 years. Eight were members of one family group; two were members of another family; three were unrelated to them or to

each other. In none of the patients was there evidence of iodine deprivation or of the action of any known goitrogen.

The thyroid glands accumulated radio-iodine more rapidly than normal and in excessive amounts, which were not discharged by potassium thiocyanate. The total plasma radio-activity and the protein-bound iodine levels were above normal and within the range usually considered diagnostic of hyperthyroidism. In two patients the plasma was examined by a butanol extraction method, which revealed persisting radio-activity in the butyl alcohol extract although it was at a lower level than in the protein-bound iodine. This finding indicated that only some of the protein-bound iodine in these patients was diiodotyrosine; the chemical basis of the remainder was unknown. It could not be thyroxine because the patients responded normally to thyroid treatment. By contrast, the urine excretion levels of radio-iodine were those usually found in hypothyroidism.

These findings indicated that the thyroid glands of these goitrous cretins were able to take up inorganic iodine from the blood and convert it into an organic form. An organic iodine compound, not thyroxine, was then released into the circulation. It was then excreted in the urine, presumably because it could not be utilized by the tissues. It was suggested that in the 12 patients there was an intrinsic, possibly familial, defect in the final synthesis of the thyroid hormone.

DR. JAMES CROOKS (London). 'Non-inflammatory Laryngeal Stridor in Infants.' To be published in full.

DR. JOHN APLEY (Bristol). 'The Infant with Stridor: a Follow-up Survey of 80 Cases.' Because in infants with stridor so little has been recorded apart from laryngeal abnormalities, in this survey the emphasis was on the patient rather than the larynx. In 80 consecutive cases with stridor from early infancy mental and physical assessments were repeated at intervals for periods up to several years.

There was a moderately high familial incidence, with 11 siblings affected in five families. In the whole series there was a preponderance of males (50 boys to 30 girls). The average birth weight of males with stridor was significantly higher than that of females with stridor or of unselected infants. Seven patients had congenital heart disease, and 16 were mentally defective, though the only criterion of selection was the occurrence of stridor. The surprisingly high incidence of these associated anomalies was not apparent at the earliest examinations but became established during the follow-up period. Chest deformities were common but almost invariably transient. Irrespective of the cause of stridor, pulmonary complications occurred frequently and were often serious. In this series 11 patients, with stridor of varying aetiology, died (eight with pulmonary complications), and in 10 post-mortem examination was carried out.

DR. D. V. HUBBLE (Derby). 'Some Disorders of Growth in Childhood.' A boy with presumed hypopituitary dwarfism had been given 20 units of protamine zinc insulin over a period of three months. No growth occurred, but he gained 14 lb. with considerable deposition of fat. Best has shown that protamine zinc insulin will produce normal growth in hypophysectomized rats. It was assumed that in the presence of corticosteroids insulin increased lipogenesis but did not encourage protein deposition. Insulin, however, in an eight-day balance, produced considerable nitrogen retention. It was shown in a boy with glycogen storage disease by eight-day nitrogen balances that a high protein intake with a night feed of protein caused nitrogen retention where nitrogen deficit had previously been demonstrated. Protein breakdown occurs in glycogen storage disease because there is a deficiency of available carbohydrate for nocturnal endogenous metabolism. It was suggested that a similar nocturnal protein breakdown occurs in some children with diabetes when long-acting insulins are not used. Three cases of the Mauriac syndrome were described (dwarfism, obesity, hepatomegaly from glycogen deposit, and 'full-moon' face), and it was shown, again by nitrogen balances, that the protein breakdown could be corrected either by long-acting insulin or by a high protein diet.

DR. R. E. SMITH (Rugby). 'Improvements to Mechanical Respirators.' Improvements to both respirators as reported in the *Lancet* of April 4, 1953 were described. Since then a new device facilitating the change, if necessary, from electrically driven to manual pumping had been added.

Further improvements were unlikely and two different new types were described. The first was the so-called 'alligator', the upper half of which could be raised on a hinge at the end, and the patient could be nursed in the prone and supine positions. Access to the patient was much simpler. The second was a cylindrical respirator containing a bed which was pulled out as in the 'both' respirator. This could be revolved through 180° so that the patient if slung in a hammock could be turned painlessly when postural drainage was desired.

The models produced were made by Captain G. T. Smith-Clarke who had freely given of his time and his engineering skill. The second type described was inspired by Dr. W. H. Kelleher.

DRS. H. M. M. MACKAY and B. LEVIN (London). 'Human Milk and Dried Cow's Milk as Foods for Premature Babies: Protein Intake and Growth.' This communication was concerned with the progress during the early weeks of life of babies under 4½ lb. at birth. Their rate of increase in weight after birth (those on human milk and on dried milk combined) was very similar to that normally occurring *in utero*. Their serum protein levels rose more rapidly than those of full term infants. However, when subdivided according to feeding, the mean weekly gain of babies receiving half or more of their total calorie intake in the form of sweetened half-cream dried milk was about 45% greater than that of those fed exclusively on breast milk from birth. Grouped according to their protein intake per lb. body weight per day, and excluding the first two weeks of life, babies receiving under 1·7 g. per pound had a poorer gain in weight than those having 1·7 g. and upwards; and, if protein was the sole limiting factor in growth, the requirement must be about 1·7 g. lb. per day. Among babies receiving less than 1·5 g. protein per lb. the gain in weight was poorest among those of lowest birth weight.

The mineral content of human milk is also inadequate for small premature babies, since Von Sydow has shown that premature babies fed on breast milk plus vitamin D are more liable to rickets than those on cow's milk plus vitamin D. More information is necessary regarding susceptibility to infection, but it is probable that after their first week of life a supplement of processed cow's milk is desirable, even when breast milk is available, for all small premature babies.

DR. JOHN L. EMERY (Sheffield). 'Changes in the Liver in the Newborn related to Physiological Icterus.' There is microscopical evidence of a generalized degeneration of the parenchymal cells of the left physiological lobe of the liver in about a third of children dying in the first 48 hours of life.

Livers of premature infants and those dying after birth were divided into their physiological lobes. The ratios of the weights of the lobes were obtained. It was found that there was a rapid alteration in ratio of the size of the left and right lobes beginning at birth and complete within 10 days of birth. This was due to a rapid diminution in weight of the left liver.

This liver change may be explained on two bases. First, the sudden alteration at birth in the blood supply to the liver; *in utero* the left liver receives blood direct from the placenta and this source of oxygenated blood suddenly ceases at birth. Second, the persistence in many infants of a functioning ductus venosus for a short time after birth.

It is suggested that the acute involution of the left liver described is a probable cause of the transitory hepatic inadequacy immediately following birth and the cause of physiological icterus.

DR. R. J. PUGH (Leeds). 'Liver Damage and Congenital Galactosaemia: An Attempt at Clinico-pathological Correlation.' Three examples were described, all presenting in the first week of life with anorexia, drowsiness and vomiting. There was an excessive initial weight loss and progressive hepatomegaly with evidence of disturbed liver function. The earliest case ran its course over four weeks, unmodified by lactose omission, to terminate with clinical and histological evidence of liver failure with cirrhosis. Clinical progress in the two other patients was modified by lactose omission with dramatic subjective improvement, and with objective evidence of more adequate liver function, but without prolonging life beyond two months and three months respectively. Comparison of the liver histology of the treated cases with the unmodified one showed that at necropsy the former demonstrated relatively insignificant structural damage. In addition, the most recent example was subjected to liver biopsy before lactose omission revealing extensive early pericellular fibrosis, which had undergone remarkable resolution by the time of death eight weeks later. The cause of the hepatomegaly was seen at biopsy to be attributable to fatty change in the parenchyma and not to glycogen deposition, which was scanty. Both treated cases exhibited a gross aminoaciduria throughout life without modification when liver function improved.

DR. MARTIN BODIAN (London). 'Some Observations on Children with Cytomegalic Inclusions.' The morphological features of the cytomegalic inclusions in nucleus and cytoplasm were discussed and their finding in the salivary glands of 10% or more of stillborn and liveborn children regardless of the cause of death was noted. The inclusions in these tissues of predilection cause no symptoms and are presumed to reflect a carrier state of the salivary gland virus.

More or less widespread haematogenous dissemination of the virus is found in about 1% of all children's necropsies. Nine cases of the disseminated disease were presented. The pathological and clinical manifestations of this condition may be erythroblastosis foetalis with purpura in the absence of blood group incompatibility, neonatal hepatitis, interstitial nephritis, interstitial pneumonitis, encephalomyelitis with encephalomalacia sometimes leading to hydrocephalus and focal calcification of the brain, myocarditis, and other features are seen more rarely. The predisposition to disseminated

cytomegalic inclusion disease in debilitating disorders, such as diarrhoea and vomiting, bacterial infections especially pertussis, and fibrocystic disease of the pancreas was also noted.

MR. R. B. ZACHARY (Sheffield). 'The Non-Operative Reduction of Intussusception.' A method for the non-operative reduction of intussusception, employing a barium enema under x-ray screen was described. Some excellent results had been obtained by this means and the difficulties and dangers of the method were discussed.

DR. W. WALKER (Newcastle upon Tyne). 'Studies in the Incidence, with Results in Haemolytic Disease of the Newly Born.' The incidence of haemolytic disease of the newborn in the North of England is probably 5 per 1,000 total births.

Ten per cent. of all affected infants are stillborn whether first affected or not, and whether the mother has been immunized by pregnancy or transfusion. Of the liveborn infants, 40% recover without transfusion whereas 60% require treatment sooner or later.

The 'Newcastle cases' that formed part of the national investigation provided a valid comparison between exchange and simple transfusion in the babies of mothers allowed to go to spontaneous delivery. Exchange is significantly superior to simple transfusion both as regards survival and the prevention of kernikterus.

It is recommended that all babies likely to be affected should be delivered in hospitals providing special facilities for their care, and all requiring treatment should be treated by early exchange transfusion. The following criteria for exchange transfusion were suggested: (1) Cord Hb. value 14·8 g. or less; (2) cord Hb. value 14·9 to 17·7 g. associated with cord bilirubin value of more than 2·7 mg.%.

With this machinery working relatively smoothly, 109 liveborn affected babies were born in the Newcastle group of hospitals in 1952. Sixty were treated by early exchange transfusion, five by late simple transfusion, while 44 survived without treatment. No baby left without early treatment died. There were three deaths in the exchange group but two of these deaths were in premature babies moribund at birth with Hb. values of 4 g. and therefore regarded as non-viable.

Two hundred babies were treated by exchange transfusion with an overall survival rate of 86%. There was only one case of kernikterus in a mature baby, whereas four out of 15 premature babies treated by adequate early exchange developed kernikterus.

PROFESSOR W. GAISFORD (Manchester). 'B.C.G. Vaccination in the Newborn.' The pros and cons of B.C.G. vaccination in the newborn were discussed and the results reported of some 4,000 infants vaccinated in the past three years. As tuberculous meningitis was most dangerous in the first two years of life, and as experience had shown the success of B.C.G. vaccination in the prevention of tuberculous meningitis, it was logical that, if protection was to be provided, it should be given as soon after birth as possible.

The results showed that successful vaccination had been obtained in 100% of newborn infants and that only half the dose used for older children was necessary. The response varied with the type of vaccine used. With Swedish and freeze-dried vaccine the results were less certain, the reactions less marked and the conversion time longer. With Danish vaccine successful conversion had been obtained in as little as 14 days with 0·05 ml. of vaccine.

Complications were so frequent when the inoculations were made in the thigh that they were soon discontinued. With injections into the arm in the region of the insertion of the deltoid muscle the incidence of complications had been reduced to 0·3%. No serious or systemic complications had been encountered; local abscesses, regional adenitis and abscess formation were the only untoward occurrences. Calcification in the axillary, supraclavicular and inguinal glands was a common finding some months after vaccination, but no case of hilar calcification had been seen.

All the infants examined at the first yearly follow-up were still tuberculin positive and no deaths from tuberculosis had occurred in vaccinated infants during this period.